PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 22 August 2001 (22.08.01)	
International application No. PCT/US00/25157	**Applicant's or agent's file reference** 887-4149PC1
International filing date (day/month/year) 14 September 2000 (14.09.00)	**Priority date** (day/month/year) 14 September 1999 (14.09.99)

Applicant

BARBOUR, Randall, L. et al

1. The designated Office is hereby notified of its election made:

   [X] in the demand filed with the International Preliminary Examining Authority on:

   04 April 2001 (04.04.01)

   [ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

   [ ] was not

   made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer CRUZ Juan
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

INTERNATIONAL SEARCH REPORT

A.	CLASSIFICATION OF SUBJECT MATTER

IPC(7)   :G01N 21/00; H01J 3/14
US CL   :356/436; 250/216

According to International Patent Classification (IPC) or to both national classification and IPC

B.	FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. :   356/436; 250/216

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

USPTO EAST

C.	DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A,P	US 5,994,690 A (Kulkarni et al) 30 November 1999 (30/11/99), see entire document.	1-23

☐ Further documents are listed in the continuation of Box C.   ☐ See patent family annex.

	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance		
"E"	earlier document published on or after the international filing date	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed	"&"	document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
02 NOVEMBER 2000	09 JAN 2001

Name and mailing address of the ISA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	MICHAEL P. STAFIRA
Facsimile No. (703) 305-3230	Telephone No. (703) 308-4837

Form PCT/ISA/210 (second sheet) (July 1998)★

PATENT COOPERATION TREATY

To: KURT E. RICHTER
MORGAN & FINNEGAN, L.L.P.
345 PARK AVENUE
NEW YORK NY 10154-0053

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Date of Mailing (day/month/year)	**09 JAN 2001**

Applicant's or agent's file reference	FOR FURTHER ACTION See paragraphs 1 and 4 below
887-414PC1	

International application No.	International filing date (day/month/year)
PCT/US00/25157	14 SEPTEMBER 2000

Applicant
THE RESEARCH FOUNDATION OF STATE UNIVERSITY OF NEW YORK

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1. [X] The applicant is hereby notified that the international search report has been established and is transmitted herewith.

   Filing of amendments and statement under Article 19:
   The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

   When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.

   Where? Directly to the International Bureau of WIPO
   34, chemin des Colombettes
   1211 Geneva 20, Switzerland
   Facsimile No.: (41-22) 740.14.35

   For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. [ ] With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

   [ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

   [ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):**   The applicant is reminded of the following:

   Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 *bis* 1 and 90 *bis* 3, respectively, before the completion of the technical preparations for international publication.

   Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

   Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	MICHAEL P. STAFIRA
Facsimile No. (703) 305-3230	Telephone No. (703) 308-4837

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 887-414PC1	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US00/25157	International filing date *(day/month/year)* i4 SEPTEMBER 2000	(Earliest) Priority Date *(day/month/year)* 14 SEPTEMBER 1999

Applicant THE RESEARCH FOUNDATION OF STATE UNIVERSITY OF NEW YORK

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of _3_ sheets.

   [X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

    a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

       [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

    b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

       [ ] contained in the international application in written form.

       [ ] filed together with the international application in computer readable form.

       [ ] furnished subsequently to this Authority in written form.

       [ ] furnished subsequently to this Authority in computer readable form.

       [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the

       [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. [ ] Certain claims were found unsearchable (See Box I).

3. [ ] Unity of invention is lacking (See Box II).

4. With regard to the title,

       [X] the text is approved as submitted by the applicant.

       [ ] the text has been established by this Authority to read as follows:

5. With regard to the abstract,

       [ ] the text is approved as submitted by the applicant.

       [X] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No. _1_

       [X] as suggested by the applicant.   [ ] None of the figures.

       [ ] because the applicant failed to suggest a figure.

       [ ] because this figure better characterizes the invention.

(handwritten annotation:) CASE 0887-4149 PC1 ATTY EDM DUE February 9, 2001 (Comm. to Abst.) 2wk. 1mo. call-up January 24, 2001 BY J.M.

INTERNATIONAL SEARCH REPORT

Box III   TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

The technical features mentioned in the abstract do not include a reference sign between parentheses (PCT Rule 8.1(d)).

NEW ABSTRACT

The present invention recongnizes that contrary to intuitive expectations, sensitivity and resolution of the data for image reconstruction can be increased by decreasing the absorption or scattering mean free path length of the imaging source energy. Methods are disclosed in this respect for enhancing sensitivity and resolution in the imaging of scattering target media (116). In one method, source energy wavelength is selected to optimize scattering and absorption of the energy while maintaining measureable and acceptable detector signals (112). In another aspect of the invention, the scattering target medium (116) is radially compressed and the imaging source wavelength is then adjusted in conjuction with the compression to improve sensitivity and resolution.

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :G01N 21/00; H01J 3/14

US CL :356/436; 250/216

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 356/436; 250/216

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

USPTO EAST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A,P	US 5,994,690 A (Kulkarni et al) 30 November 1999 (30/11/99), see entire document.	1-23

☐ Further documents are listed in the continuation of Box C.   ☐ See patent family annex.

*	Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	
"E"	earlier document published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means	
"P"	document published prior to the international filing date but later than the priority date claimed	"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
02 NOVEMBER 2000	09 JAN 2001

Name and mailing address of the ISA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	MICHAEL P. STAFIRA
Facsimile No. (703) 305-3230	Telephone No. (703) 308-4837

Form PCT/ISA/210 (second sheet) (July 1998)★

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: KURT E. RICHTER MORGAN & FINNEGAN, L.L.P. 345 PARK AVENUE NEW YORK NY 10154-0053	**PCT** NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT (PCT Rule 71.1)
	Date of Mailing *(day/month/year)* **27 JUL 2001**

Applicant's or agent's file reference 0887-414PCl	**IMPORTANT NOTIFICATION**

International application No. PCT/US00/25157	International filing date *(day/month/year)* 14 SEPTEMBER 2000	Priority Date *(day/month/year)* 14 SEPTEMBER 1999

Applicant THE RESEARCH FOUNDATION OF STATE UNIVERSITY OF NEW YORK

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

   The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

   Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

   For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer MICHAEL P. STAFIRA Telephone No. (703) 308-4837

Form PCT/IPEA/416 (July 1992)★

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 0887-414PC1	**FOR FURTHER ACTION** See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/25157	International filing date *(day/month/year)* 14 SEPTEMBER 2000	Priority date *(day/month/year)* 14 SEPTEMBER 1999
International Patent Classification (IPC) or national classification and IPC IPC(7): G01N 21/00; H01J 3/14 and US Cl.: 356/436; 250/216		
Applicant THE RESEARCH FOUNDATION OF STATE UNIVERSITY OF NEW YORK		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of __3__ sheets.

    ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

    These annexes consist of a total of __⊘__ sheets.

3. This report contains indications relating to the following items:

    I   ☒ Basis of the report

    II ☐ Priority

    III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability

    IV ☐ Lack of unity of invention

    V   ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

    VI ☐ Certain documents cited

    VII ☐ Certain defects in the international application

    VIII ☐ Certain observations on the international application

Date of submission of the demand 04 APRIL 2001	Date of completion of this report 28 JUNE 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer MICHAEL P. STAFIRA Telephone No. (703) 308-4837

Form PCT/IPEA/409 (cover sheet) (July 1998)★

I. Basis of the report

1. With regard to the elements of the international application:*

[X] the international application as originally filed

[X] the description:

pages   1-38   , as originally filed

pages   NONE   , filed with the demand

pages   NONE   , filed with the letter of _____

[X] the claims:

pages   39-43   , as originally filed

pages   NONE   , as amended (together with any statement) under Article 19

pages   NONE   , filed with the demand

pages   NONE   , filed with the letter of _____

[X] the drawings:

pages   1-16   , as originally filed

pages   NONE   , filed with the demand

pages   NONE   , filed with the letter of _____

[X] the sequence listing part of the description:

pages   NONE   , as originally filed

pages   NONE   , filed with the demand

pages   NONE   , filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/ or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages _____ NONE

[X] the claims, Nos. _____ NONE

[X] the drawings, sheets/fig _____ NONE

5. [ ] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

**Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	1-23		YES
	Claims	NONE		NO
Inventive Step (IS)	Claims	1-23		YES
	Claims	NONE		NO
Industrial Applicability (IA)	Claims	1-23		YES
	Claims	NONE		NO

2. citations and explanations (Rule 70.7)

Claims 1-23 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest a method for collecting data for use in an image reconstruction of a scattering target medium wherein selecting at least one wavelength of energy to maximize the total path length of energy propagating from the source to a detector and to maintain an acceptable energy density at the detector.

-------------------- NEW CITATIONS --------------------
NONE

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

14

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 0887-414PC1	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/25157	International filing date *(day/month/year)* 14 SEPTEMBER 2000	Priority date *(day/month/year)* 14 SEPTEMBER 1999

International Patent Classification (IPC) or national classification and IPC IPC(7): G01N 21/00; H01J 3/14 and US Cl.: 356/436; 250/216

Applicant THE RESEARCH FOUNDATION OF STATE UNIVERSITY OF NEW YORK

---

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of __3__ sheets.

    ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

    These annexes consist of a total of __/2__ sheets.

3. This report contains indications relating to the following items:

    I   ☒ Basis of the report

    II ☐ Priority

    III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability

    IV ☐ Lack of unity of invention

    V   ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

    VI ☐ Certain documents cited

    VII ☐ Certain defects in the international application

    VIII ☐ Certain observations on the international application

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Date of submission of the demand 04 APRIL 2001	Date of completion of this report 28 JUNE 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington. D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer MICHAEL P. STAFIRA Telephone No. (703) 308-4837

Form PCT/IPEA/409 (cover sheet) (July 1998)*

International application No.

PCT/US00/25157

I. Basis of the report

1. With regard to the elements of the international application:*

[X] the international application as originally filed

[X] the description:

pages _____ 1-38 _____ , as originally filed

pages _____ NONE _____ , filed with the demand

pages _____ NONE _____ , filed with the letter of _____

[X] the claims:

pages _____ 39-43 _____ , as originally filed

pages _____ NONE _____ , as amended (together with any statement) under Article 19

pages _____ NONE _____ , filed with the demand

pages _____ NONE _____ , filed with the letter of _____

[X] the drawings:

pages _____ 1-16 _____ , as originally filed

pages _____ NONE _____ , filed with the demand

pages _____ NONE _____ , filed with the letter of _____

[X] the sequence listing part of the description:

pages _____ NONE _____ , as originally filed

pages _____ NONE _____ , filed with the demand

pages _____ NONE _____ , filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/ or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages _____ NONE _____

[X] the claims, Nos. _____ NONE _____

[X] the drawings, sheets/fig _____ NONE _____

5. [ ] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

**Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

Form PCT/IPEA/409 (Box I) (July 1998)*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citati ns and explanations supporting such statement

1. statement

Novelty (N)	Claims	1-23	YES
	Claims	NONE	NO
Inventive Step (IS)	Claims	1-23	YES
	Claims	NONE	NO
Industrial Applicability (IA)	Claims	1-23	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1-23 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest a method for collecting data for use in an image reconstruction of a scattering target medium wherein selecting at least one wavelength of energy to maximize the total path length of energy propagating from the source to a detector and to maintain an acceptable energy density at the detector.

-------------------- NEW CITATIONS --------------------
NONE

(54) Title: METHOD AND SYSTEM FOR ENHANCED IMAGING OF A SCATTERING MEDIUM

(57) Abstract: The present invention recognizes that contrary to intuitive expectations, sensitivity and resolution of the data for image reconstruction can be increased by decreasing the absorption or scattering mean free path length of the imaging source energy. Methods are disclosed in this respect for enhancing sensitivity and resolution in the imaging of scattering target media (116). In one method, source energy wavelength is selected to optimize scattering and absorption of the energy while maintaining measurable and acceptable detector signals (112). In another aspect of the invention, the scattering target medium (116) is radially compressed and the imaging source wavelength is then adjusted in conjunction with the compression to improve sensitivity and resolution.

— *Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.*

For two-letter codes and other abbreviations. refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

CORRECTED VERSION

10/088185

[Continued on next page]

(54) Title: METHOD AND SYSTEM FOR ENHANCED IMAGING OF A SCATTERING MEDIUM

(57) Abstract: The present invention recognizes that contrary to intuitive expectations, sensitivity and resolution of the data for image reconstruction can be increased by decreasing the absorption or scattering mean free path length of the imaging source energy. Methods are disclosed in this respect for enhancing sensitivity and resolution in the imaging of scattering target media (116). In one method, source energy wavelength is selected to optimize scattering and absorption of the energy while maintaining measurable and acceptable detector signals (112). In another aspect of the invention, the scattering target medium (116) is radially compressed and the imaging source wavelength is then adjusted in conjunction with the compression to improve sensitivity and resolution.

WO 01/020307 A1

IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report*

(48) Date of publication of this corrected version:

26 September 2002

(15) Information about Correction:

see PCT Gazette No. 39/2002 of 26 September 2002, Section II

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

METHOD AND SYSTEM FOR ENHANCED IMAGING OF A SCATTERING MEDIUM

This application claims the benefit under 35 U.S.C. §120 of prior U.S. Provisional Patent Application Serial No. 60/153,769 filed September 14, 1999, entitled TOMOGRAPHY IN A SCATTERING MEDIUM.

Field of the Invention

10   The invention relates to the field of imaging in a scattering medium, and more particularly to optimization of source parameters to enhance the resolution and sensitivity of measured data and the reconstructed image of the medium.

Background of the Invention

Imaging in a scattering medium relates generally to the methods and techniques of

15   generating an image of the internal properties of a scattering medium on the basis of detected scattered energy.

Many systems and techniques have been developed for imaging of scattering media. A typical system for imaging based on scattered energy detection includes a source for directing energy into a target medium and at least one detector, at one or more

20   locations with respect to the source, for measuring the scattered energy exiting the target medium. From these measurements of energy exiting the target medium, it is possible to reconstruct images that represent the scattering and absorption properties of the target.

The absorption and scattering properties of the medium are a function of the medium itself, and of the wavelength and type of energy employed as an imaging source.

Exemplary methods and systems for imaging of a scattering media are disclosed in Barbour et al., U.S. Patent No. 5,137,355, entitled "Method of Imaging a Random

5   Medium," (hereinafter the "Barbour '355 patent"), Barbour, U.S. Patent No. 6,081,322, entitled "NIR Clinical Opti-Scan System," (hereinafter the "Barbour '322 patent"), copending application serial number "not yet assigned," attorney docket number 0887-4147PC1, filed on the same day as this application, entitled "SYSTEM AND METHOD FOR TOMOGRAPHIC IMAGING OF DYNAMIC PROPERTIES OF A SCATTERING

10   MEDIUM" by inventors R. L. Barbour and C. H. Schmitz (hereinafter the "Barbour 4147PC1 application"), copending application serial number "not yet assigned", attorney docket number 0887-4149PC1, filed on the same date as this application, entitled "METHOD AND SYSTEM FOR IMAGING THE DYNAMICS OF A SCATTERING MEDIUM" by inventor R. Barbour and is hereby incorporated by reference (hereinafter

15   the "Barbour 4147PC2 application").

Imaging techniques based on these known systems and techniques measure the internal absorption and scattering properties of a medium using sources whose propagating energy is highly scattered. This permits the use of wavelengths and types of energy not suitable for projection imaging techniques. Thus these techniques have great

20   potential for detecting properties of media that are not accessible to energy sources used for projection imaging techniques (e.g., x-rays).

As can readily be appreciated, there are many instances where these techniques are highly desirable. For example, one flourishing application is in the field of optical

tomography. Optical tomography typically uses near infrared radiation (i.e., electromagnetic radiation with wavelengths in the range of ~750–~1200 nanometers) as an energy source. Near infrared radiation is highly scattered in human tissue and is therefore an unsuitable source for practical projection imaging in the human body.

5   However, these properties make near infrared radiation a superior imaging source for scattering imaging techniques. The ability to use near infrared radiation as an imaging source is of particular interest in the human body because the strength of the interactions between the radiation and tissue are exceptionally responsive to blood oxygenation levels and blood volumes. These attributes permit imaging of the vasculature, and thus provide

10   great potential for detecting cardiovascular disease, tumors and other disease states.

        Of central importance to these and other imaging methods is an appreciation of the limits of sensitivity and achievable resolution of the reconstructed image. In the case of simple projection imaging, the properties of the point-spread function largely determine the sensitivity and resolution limits. In model-based techniques for imaging of

15   scattering media, sensitivity and resolution are strongly influenced by a complex relationship between a host of parameters associated with the target properties (i.e., target domain), conditions and quality of collected data (i.e., measurement domain) and stability and accuracy of numerical methods used for image recovery (i.e., analysis domain). However, sensitivity and resolution are ultimately limited by the quality of the collected

20   data. Known methods and systems for imaging of scattering media provide images having relatively low resolution and sensitivity.

For the foregoing reasons, there is an ongoing need for methods of improving the quality of the data collected from a scattering medium in a manner that enhances the resolution and sensitivity of the reconstructed image.

SUMMARY OF THE INVENTION

5   The present invention satisfies this need by (1) recognizing that, contrary to expectations, resolution and sensitivity can be improved by decreasing the mean free path length of the measured energy travelling through the medium, (2) providing a method for enhancing the resolution and sensitivity by selecting wavelengths of energy that increase the total path length (i.e., minimum distance the energy must travel, expressed as

10   multiples of the mean free path length) of the energy through the medium, and (3) providing a method for enhancing resolution and sensitivity by radially compressing the target medium in conjunction with wavelength selection.

It is one object of the present invention to provide a method for collecting data for use in image reconstruction of a target medium so that the resolution and sensitivity of

15   the reconstructed image are enhanced. The method comprises providing a source and a detector, selecting one or more wavelengths of energy, directing the selected wavelength(s) of energy into the target medium and measuring the energy emerging from the target. Selecting the wavelength(s) comprises selecting one or more wavelengths of energy so that the total path length of the energy propagating through a target medium

20   between a source and a detector is maximized.

It is a further object of the present invention to provide a plurality of detectors at a plurality of distances from the source and to select a plurality of wavelengths of energy, to enhance the resolution and sensitivity of the reconstructed image of the target. The

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plurality of wavelengths of energy are selected so that each of the plurality of wavelengths maximizes the total path length of energy between a source and at least one detector.

5   It is yet a further object of the invention to provide a method of selecting an optimal wavelength of energy to maximize the total path length. The method comprises providing a source and a detector, directing a wavelength of energy from the source into a target medium, measuring the emerging energy using at least one detector, and adjusting the wavelength of energy until the total path length is maximized, under the constraint that the energy density at the detector remains at an acceptably large value.

10   It is yet another object of the invention to further enhance resolution and sensitivity by radially compressing the target medium prior to wavelength selection, whereby compression of the tissue reduces the physical distance between a source and detector, and selection of an optimal wavelength increases the total path length so that resolution and sensitivity are increased.

15   **BRIEF DESCRIPTION OF THE FIGURES**

For a better understanding of the invention, together with the various features and advantages thereof, reference should be made to the following detailed description of the preferred embodiments and to the accompanying drawings, wherein:

FIG. 1 is a schematic illustration of an exemplary imaging system;

20   FIG. 2 is an illustration of an optimal wavelength approach;

FIG. 3 is an illustration of a combination of radial compression and optimal wavelength approaches;

FIG. 4A is a reconstructed image of a coronal slice of a breast derived from MRI

maps;

FIG. 4B is a finite element model (FEM) of the coronal slice in FIG. 4A;

FIG. 5 is an illustration of the data acquisition geometry for a full tomographic

5   view with 36 detectors in a uniform ring geometry, 9 detectors are illustrated;

FIG. 6 is an illustration of the parameters used to define edge resolution;

FIG. 7 is a graph plotting the percent change in relative sensitivity versus view

angle for different target sizes;

FIG. 8A is a graph plotting the percentage change in relative sensitivity versus the

10   cross-sectional area ratio for different breast diameters;

FIG. 8B is a graph plotting the percentage change in relative sensitivity versus the

breast diameter for different cross-sectional area ratios;

FIG. 9A is a graph plotting EFWHM versus the cross-sectional area ratio for

different breast diameters;

15   FIG. 9B is a graph plotting EFWHM versus the breast diameter for different

cross-sectional area ratios;

FIG. 10A is a graph plotting EFWHM versus the maximum sensitivity change

caused by variations of breast and tumor size in homogeneous background media, where

the absorption coefficient is fixed at 0.08 cm^{-1} and the scattering coefficient varies from

20   10 to 40 cm^{-1};

FIG. 10B is a graph plotting EFWHM versus the maximum sensitivity change

caused by variations of breast and tumor size in homogeneous background media, where

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the absorption coefficient is fixed at 0.2 cm^{-1} and the scattering coefficient varies from 10

to 40 cm^{-1};

FIG. 10C is a graph plotting EFWHM versus the maximum sensitivity change

caused by variations of breast and tumor size in homogeneous background media, where

5   the scattering coefficient of tumor is fixed at 10 cm^{-1} and the absorption coefficient varies

from 0.08 to 0.04 cm^{-1};

FIG. 11 is a graph plotting sensitivity versus view angle for different

heterogeneous background media with a breast size of d = 16 cm, tumor size of r =

0.25%, and case 1 tumor contrast;

10   FIG. 12 is a graph plotting sensitivity versus view angle for different breast sizes,

with case 3 tumor contrast and tumor size of r = 1%, embedded in case 6 heterogeneous

background medium;

FIG. 13A is a graph plotting the ratio of sensitivity at $180°$ view angle to that at

$200°$ view angle, versus the cross-sectional area ratio for different breast diameters;

15   FIG. 13B is a graph plotting the ratio of sensitivity at $180°$ view angle to that at

$200°$ view angle, versus the breast diameter for different cross-sectional area ratios, with

case 6 heterogeneous background tissue and case 3 tumor contrast;

FIG. 14A is a graph plotting the ratio of the maximum relative intensity changes

caused by source 1 ($\theta = 0°$) and source 2 ($\theta = -40°$) versus the cross-sectional area ratio,

20   for different breast diameters;

FIG. 14B is a graph plotting the ratio of the maximum relative intensity changes

caused by source 1 ($\theta = 0°$) and source 2 ($\theta = -40°$) versus the breast diameter, for

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different cross-sectional area ratios, with case 6 background tissue and case 3 tumor contrast;

FIG. 15A is a graph plotting the ratio, at 180° view angle, of relative sensitivity change for case 6 background medium to that for a homogeneous background medium

5   (case 1), versus the cross-sectional area ratio for different breast diameters (Definition of symbols provided in FIG. 8A);

FIG. 15B is a graph plotting the ratio at 180° view angle, of relative sensitivity change for case 6 background medium to that for a homogeneous background medium (case 1), versus the breast diameter, for different cross-sectional area ratios, with case 3

10   tumor contrast (Definition of symbols provided in FIG. 8B);

FIG. 16A is a graph plotting EFWHM versus sensitivity at 180° view angle for many combinations of breast size and tumor size, for a case 6 background medium and with the absorption coefficient fixed at 0.08 cm^{-1} and the scattering coefficient varying from 10 to 40 cm^{-1};

15   FIG. 16B is a graph plotting EFWHM versus sensitivity at 180° view angle, for many combinations of breast size and tumor size, for a case 6 background medium and with the absorption coefficient fixed at 0.2 cm^{-1} and the scattering coefficient varying from 10 to 40 cm^{-1};

FIG. 16C is a graph plotting EFWHM versus sensitivity at 180° view angle for

20   many combinations of breast size and tumor size, for a case 6 background medium and with the absorption coefficient varying from 0.08 to 0.4 cm^{-1} and the scattering coefficient fixed at 10 cm^{-1};

FIG. 17A is a graph plotting the percent relative change in intensity versus view

angle for different breast diameters, with case 8 tumor contrast, tumor-to-breast area ratio

r = 1%, and homogenous background media;

FIG. 17B is a graph plotting the percent relative change in intensity versus view

5   angle for different breast diameters, with case 8 tumor contrast, tumor-to-breast area ratio

r = 1%, and case 4 background media;

FIG. 17C is a graph plotting the percent relative change in intensity versus view

angle for different breast diameters, with case 8 tumor contrast, tumor-to-breast area ratio

r = 1%, and case 5 background media; and

10   FIG. 17D is a graph plotting the relative change in intensity versus view angle for

different breast diameters, with case 8 tumor contrast, tumor-to-breast area ratio r = 1%,

and case 8 background media.

DETAILED DESCRIPTION

As discussed above, the method of the present invention recognizes that, contrary

15   to intuitive expectations, decreasing the mean free path length, for either absorption or

scattering, of the imaging source energy through the target medium can improve

resolution and sensitivity of the measured data and reconstructed images. The inventive

method involves the selection of wavelengths of energy that increase the scattering and/or

absorption coefficients of energy in the medium while maintaining a measurable and

20   acceptable energy density at the detector for image reconstruction. A further aspect of

the invention involves radially compressing the target medium in conjunction with

wavelength selection to enhance resolution and sensitivity.

System

Exemplary methods and systems for imaging of scattering media are disclosed in the "Barbour '355 patent, the "Barbour '322 patent, and the Barbour 4147PC2 application. A schematic illustration of one exemplary optical system is shown in FIG. 1.

5   This system includes a computer 102, energy sources 104, 106, a source demultiplexer 108, an imaging head 110, detectors 112, and a data acquisition board 114.

A target 116 placed in the imaging head 110 is exposed to optical energy from the sources 104, 106. The optical energy originating from energy sources 104, 106 is combined by beam splitter 118 and is delivered to source demultiplexer 108. Although

10   two energy sources 104, 106 are shown in this embodiment, an unlimited number of energy sources, each having a different wavelength, can be employed. Moreover, a single variable-wavelength energy source, such as a Ti-Sapphire laser or a tunable dye laser, can be used instead. The source demultiplexer 108, controlled by computer 102, directs the optical energy to source fibers 120 sequentially.

15   Each source fiber 120 carries the optical energy from the demultiplexer 108 to the imaging head 110, where the optical energy is directed into the target 116. The imaging head 110 contains a plurality of source fibers 120 and detector fibers 122 for transmitting and receiving light energy, respectively. Each source fiber 120 forms a source/detector pair with each detector fiber 122 in the imaging head 110 to create a plurality of

20   source/detector pairs. The optical energy entering the target 116 at one location is scattered and may emerge at any location around the target 116. The emerging optical energy is collected by detector fibers 122 mounted in the imaging head 110.

The detector fibers 122 carry the emerging energy to detectors 112. The detectors 112 measure the intensity of the collected energy and generate a corresponding electrical

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signal. The data acquisition board 114 receives the signal, separates it by wavelength and

samples and holds the separated signals for delivery to computer 102. The computer 102

in turn reads and stores the signal for image reconstruction.

This process is repeated, with energy delivered to each of the source fibers

5   sequentially, and the emerging optical energy measured for each source/detector fiber

pair. This process may continue over a period of time, with the computer 102 storing the

data for reconstruction of one or more images. Additionally, the system may include two

or more imaging heads for comparing one target to another. The computer 102

reconstructs an image representative of the internal optical properties of the target by

10   using known perturbation methods to solve for the properties of the medium, such as

absorption, scattering, florescence properties, and the like. It will be appreciated by those

skilled in the art that more than one computer can be used to increase data handling and

image processing speeds. The image reconstruction process may be any known

technique, such as those disclosed in the Barbour '355 patent.

15   **Wavelength Selection Method**

The method of the present invention comprises the selection of a source energy

wavelength producing the shortest mean free path length through the medium 116, from a

source fiber 120 to a detector fiber 122, while maintaining an acceptable energy density

at the detector 112. The mean free path length is the average distance a particle of energy

20   travels between successive interactions with the medium 116 as it propagates from a

source fiber 120 to a detector fiber 122. The total path length between a source and a

detector is the ratio of the physical distance (e.g., in centimeters) to the mean free path

length, i.e., it is the distance between a source and a detector expressed in units of mean

free path lengths.

The path an energy particle takes is a function of the absorption and scattering

coefficients of the medium. The absorption and scattering coefficients are the inverse of

5   the absorption and scattering mean free path lengths of the medium, respectively. These

latter properties are the average distances a particle can travel through a medium before

being scattered or absorbed. The absorption and scattering coefficients are functions of

both position in the medium and of the source energy wavelength.

As discussed above, the inventors of the present invention have discovered and

10   make use of the counterintuitive phenomenon that the resolution and sensitivity of a

reconstructed image can be increased by increasing the amount of scattering that energy

undergoes as it propagates through a target medium 116. One way to increase scattering

(and hence the total path length) is to increase the physical size of the target medium 116.

However, this frequently is not a practical option. For example, the physical dimensions

15   of living tissue, such as a human forearm, are not freely expandable. Accordingly, the

method of the present invention recognizes that a "virtual" enlargement of the target can

be created through adjustment of the wavelength of the imaging energy source. Referring

to FIG. 2, a target medium 202 is illustrated having an included object 204. The target

medium is shown at left in FIG. 2 in its physical size and at right in FIG. 2 in its "virtual"

20   size after wavelength optimization 210. The result is that the total path length between

source fiber 206 and detector fiber 208 has increased, so there has been a "virtual"

enlargement of the target medium.

This "virtual" enlargement is realized because the total path length through the medium and the density of energy emerging from it are functions of the wavelength-dependent scattering and absorption coefficients. The shorter the scattering mean free path length, the more the energy particles are scattered, resulting in a longer total path

5   length through the medium from a source to a detector. However, absorption also is a function of the total path length, with the probability of absorption increasing exponentially as the product of absorption coefficient and total path length increases. Accordingly, as the wavelength is adjusted to increase the total path length, there is more absorption of the energy particles and a lower energy density at the detectors. Thus, there

10 is a tradeoff between increasing total path length and maintaining acceptable energy density levels at the detectors.

By way of example, in a system for imaging a scattering medium using one wavelength of energy from a source and a plurality of detectors at different locations about the medium, the energy leaving the source will travel a different total path length to

15 reach each detector. Referring back to FIG. 1, assume the source fiber 120 is located at the 12 o'clock position on imaging head 116. The source fiber 120 being at the 12 o'clock position, all energy particles will enter the medium from the source at the 12 o'clock position, but may exit at any of the detector fiber 122 locations arranged around the target 116. However, a particle that propagates through the medium to a detector

20 fiber 122 at the 6 o'clock position is likely to have been scattered a far greater number of times and traveled a far greater total path length than a particle that exits at a position closer to the source fiber, such as a detector fiber at the 2 o'clock position.

As either the absorption or the scattering coefficient increases, the only photons that are likely to exit the medium into any given detector are those whose propagation paths lie close to the straight line joining the source to that detector. This preferential rejection of light that propagates from source to detector along paths other than the

5   straight line increases the sensitivity of the detector to objects that straddle the source-to-detector line. Similarly, the reduced influence on the detector of structures that lie off this line implies a sharper transition from detectors that can "see" an inclusion to those that can not, i.e., improved spatial resolution. Therefore, given for example the empirical fact that for near infrared radiation in tissue both the scattering and absorption

10   coefficients trend upward as wavelength decreases, a "virtual" enlargement of a tissue target can be accomplished simply by using a shorter illumination wavelength.

The method of the present invention may be used either to select a single optimal wavelength for single-wavelength systems, or a plurality of optimal wavelengths in multi-wavelength systems. Where a single wavelength is to be employed, it is selected so

15   that the total path length is maximized while maintaining an acceptable energy density at the detector fiber that is most distant from the source fiber (in units of mean free path lengths through the medium). In this instance, because only one wavelength is available, the wavelength is optimized for the farthest detector.

Where multiple wavelengths are available, an optimum wavelength is selected for

20   each detector or group of detectors, so that a plurality of wavelengths are selected, each wavelength being optimized for a single detector or group of detectors. In this way, the wavelengths are selected so that the total path lengths from the source to each detector are substantially equal at each detector's optimum wavelength.

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The actual wavelength selection is preferably made empirically by a scout scan of the target medium, but it will be appreciated that the selection also could be made through rigorous solutions of the radiation transport equation. The scout scan is employed to determine the optimal wavelength(s) through a trial-and-error process.

5   Where one source wavelength will be used for imaging, the trial and error scouting process includes incrementally adjusting the source wavelength until the energy density at any one of the detectors reaches the lowest acceptable level. Where multiple source wavelengths will be used for imaging, the preferred scouting method exposes the target medium to a series of wavelengths, the optimal wavelength for each detector being the

10   wavelength for which the electrical signal generated by that detector reaches the lowest acceptable level.

For example, using optical energy in the near infrared region on human tissue, it is known that the absorption and scattering coefficients of the tissue increase with decreasing wavelength, and thus the total path length increases and the signals generated

15   by the detectors decrease. Accordingly, selection of wavelengths using the scouting method could begin with a long infrared wavelength. The wavelength is then incrementally decreased, the optimal wavelength being selected for each detector as the wavelength is decreased. The optimal wavelength is the shortest wavelength before which the energy density at a detector falls to an unacceptably low level. Alternatively,

20   the method may start with a short wavelength, incrementally increasing the wavelength and selecting the optimal wavelength for each detector when the energy density at the detector becomes acceptable. An acceptable signal at the detector is one for which the associated signal-to-noise ratio is above about 10.

Accordingly, in selecting a wavelength, a balance must be sought to optimize resolution and sensitivity against a declining energy density or signal level at the detectors. As a consequence, the optimal wavelength range can be expected to vary with the physical diameter of the medium. For example, in an imaging system employing

5   primarily near infrared energy, a longer wavelength range (e.g., 800-700 nm) should be used for large diameter objects (10cm - 20cm), whereas a shorter wavelength range (e.g., 600-700nm) should be used for smaller diameter objects (2.5cm - 6.0cm). In effect, for multiple-wavelength systems, a rainbow of light colors should be used and varied to enhance sensitivity and resolution, as indicated, in accordance with the target dimensions.

10   In order to maximize the resolution- and sensitivity-enhancing methods of the present invention, energy density from the source should be selected up to the acceptable limits of the medium being imaged. In this way energy densities at the detectors will be increased, permitting increased total path length and enhanced resolution and sensitivity.

A further aspect of the present invention is radial compression of the target

15   medium. Like planar compression techniques, which apply compressive forces to opposing sides of the medium, radial compression reduces the physical distance through the medium between the source and detector by compression. Using planar compression techniques, the decreased physical thickness of the medium increases the energy density at the detectors but reduces the view angle over an embedded object within the medium.

20   However, unlike planar compression, radial compression preserves a large view angle over an embedded object, at least where the embedded object also is compressible. The radial compression technique may then be combined with the wavelength-selection method discussed above to further enhance sensitivity and resolution.

The approach of radial compression combined with optimal wavelength selection is illustrated in FIG. 3. In FIG.3, the target medium 302 is a large breast containing a small tumor 304. A source 306 and detector 308 are positioned on the boundary of the target medium 302. Exerting mild radial compression 310 using any known means, such

5   as those disclosed in the Barbour '099 application, the physical diameter of the target medium 302 is reduced, thereby increasing the energy density at detector 302. Depending on the compressibility characteristics of the tumor, imaging of the target medium in the compressed state will likely enhance sensitivity but decrease resolution of the tumor, at least in relative terms. However, by adjusting the source wavelength to

10   select the optimal wavelength or wavelengths 320 as discussed above, the total path length through the target can be increased, thereby improving both sensitivity and resolution in absolute terms. This is illustrated as a virtual enlargement of the target medium 302.

Image reconstruction in both single- and multiple-wavelength systems may be

15   accomplished by any known techniques, such as the SART or CGD methods. However, unlike single-wavelength methods for image reconstruction, the multiple-wavelength method of the present invention will generate a plurality of data sets based on the measured detector values for each wavelength. The most straightforward way to handle these data sets (i.e., the detector measurements) for each wavelength is to evaluate the

20   data for each wavelength separately, followed by coalescing of results to produce a composite image. Formally, this requires solving a perturbation formulation of the radiation transport equation for each wavelength employed, using any of the known methods, such as those disclosed in the Barbour '355 patent.

While the multi-wavelength methods of the present invention may complicate data acquisition and analysis, a nearly ten-fold increase in sensitivity is observed upon an eight-fold increase in total path length.

Although the numerous examples above, and those to be discussed below, focus

5   on near infrared energy sources for imaging human tissue, the methodology of the present invention is applicable with essentially any wavelength for any energy source (e.g., electromagnetic, acoustic, etc.), any scattering medium (e.g., body tissues, oceans, foggy atmospheres, geological strata, and various materials, etc.), and any source condition (e.g., time-independent, time-harmonic, time-resolved). Its applicability is dependent

10   only on the presence of the phenomenology described herein, (i.e., diffusion being the principal mechanism of energy transport), which is expected in all cases where scattering occurs. Accordingly, this methodology can be extended to allow for new imaging approaches in a broad range of applications, including nondestructive testing, geophysical imaging, medical imaging, and surveillance technologies.

15   **Experimental Validation**

The following discussion presents results validating the relationship of increased total path length to enhanced resolution and sensitivity using a near infrared imaging system. These examples are presented merely as an illustration of the benefits of the optimized wavelength method of the present invention.

20   The analysis herein is described as it was used to determine the interdependencies of measurement parameters, such as view angle, wavelength and source location, and target parameters such as use of contrast agents, target geometry and size, background contrast, inclusion contrast and structural heterogeneity, as they relate to the sensitivity

and edge resolution for a defined ROI. The analysis was divided into two parts: first, the

exploration of homogeneous models with a centered inclusion simulating a tumor, and,

second, examination of anatomically accurate optical (AAO) breast models, as defined by

MRI data, containing a centered "tumor." The first is included primarily to differentiate

5   the influence of geometry factors from effects of internal contrast features on the

measured response. Its simplicity also facilitates focused laboratory investigations on

phantoms for the purpose of verifying potentially interesting system performance

features.

MR images of the breast were obtained using a GE Signa MRI system to develop

10   a realistic model of the breast. The fast spin echo technique (TR = 4000 ms, TE = 112

ms, 3 mm thickness) was used, with and without fat and water suppression. A series of

24 sagittal images was obtained, and each image was subsequently converted into coronal

views using the VoxelView image display program ("VoxelView 2.5 User's Guide," Vital

Images, Inc. (www.vitalimages.com), 1995). The MRI breast maps were segmented

15   using a semi–automatic image segmentation code provided by Chris Johnson from the

University of Utah (H. W. Shen and C. R. Johnson, "Semi–automatic image

segmentation: A biomedical thresholding approach," Technical Report UUCS–94–019,

Dept. of CS, Univ. of Utah, 1994) (the disclosures of which are incorporated herein by

reference). This code permits identification of user–defined outer and inner boundaries

20   using a cubic spline data–fitting method. Referring to FIGS. 4A and 4B, FIG. 4A

illustrates a representative coronal–view map (displayed at low resolution). FIG. 4B

illustrates a corresponding representative finite element mesh of the map in FIG. 4A, with

the introduction of a central inclusion simulating a tumor. The boundary geometries of

the two maps differ because the external boundary of the breast was extended to conform

to a circular geometry in the FEM model. This simplification was adopted to reflect the

expected geometry that would exist for measurements of the breast using an imager that

conforms the breast to a known circular shape.

5   Three different tissue types are identified in the MRI: adipose, parenchyma and

the centrally positioned tumor shown in the FEM map. This central location was selected

because it represents the region most difficult to detect. The extended region was

assigned coefficients corresponding to adipose tissue. The segmented image served as

the input file for FEM mesh generation. The mesh generation code, also provided by C.

10   Johnson, uses the Delaunay tessellation algorithm originally proposed by Watson (D. F.

Watson, "Computing the n–dimensional Delaunay tesselation with applications to

Voronoi polytopes," Computer Journal 24(2), 167–172 (1981)). This algorithm was later

extended by Weatherhill (N. Weatherill, and O. Hassan "Efficient three–dimensional grid

generation using the Delaunay triangulation," Proceeding of the 1st European CFD

15   Conference, 1 (1992)) (the disclosures of which are incorporated herein by reference).

This code was implemented iteratively, with inspection of the generated mesh following

each iteration to ensure construction of a mesh without any discontinuities between

segmented regions.

The number of points and elements on the mesh used in the different models

20   varied with breast size. For small diameters, the number of the points and elements was

on the order of 1,500 and 3,000, respectively. For large diameters, these values were

increased by as much as a factor of 15. An adaptive uniform refinement method was

used to improve the efficiency of the FEM calculation for large–diameter maps (R. Beck,

B. Erdmann and R. Roitzsch, "Kaskade 3.0 - An object–oriented adaptive finite element code," Technical report TR 95–4, Konrad–Zuse–Zentrum für Informationstechnik, Berlin (1995)) (the disclosure of which is incorporated herein by reference). It is worth noting that whereas a variety of breast maps have been examined, the experimental validation

5   described uses a single MRI map. Thus, the internal structural configuration of the background tissue is identical for all breast/tumor composite geometries explored. This was done for the purpose of differentiating the influence that variations in background/tumor contrast have on the measured parameters from effects caused by variations in the composite breast/tumor geometry.

10   **Forward Model and Data Acquisition Geometry**
       The technique and method modeled light propagation in breast tissue as a diffusion process. For a domain Ω having a boundary $\partial\Omega$ and a DC point source, the diffusion process is represented by the expression:

$$\nabla \cdot \left[D(r)\nabla u(r) \right] - \mu_a(r)u(r) = -\delta(r - r_s), r \in \Omega$$

15   where $u(r)$ is the photon density at position r, r_s is the position of the point source and $D(r)$ is the position–dependent diffusion coefficient, which is related to the absorption coefficient $\mu_a(r)$ and reduced scattering coefficient $\mu_s'(r)$ by

$$D(r) = \frac{1}{3\left[\mu_a(r) + \mu_s'(r) \right]}$$

       Light intensity values at the detectors were computed by applying Dirichlet
20   boundary conditions on an extrapolated boundary. Depending on the breast size, the sources and detectors were positioned 1–2 transport mean free pathlengths below the

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extended surface. Solutions to the diffusion equation were computed by using the

KASKADE adaptive finite element method. This is a publicly available code suitable for

the solution of partial differential equations in one, two or three dimensions, using

adaptive finite element techniques. For the purposes of the present invention, the basic

5   code was modified to enable solutions to the diffusion equation with a point source.

FIG. 5 illustrates the data acquisition geometry. The arrows in the figure show

two different locations of sources used for the reported results. Whichever of the two

sources is adopted, the position of the detector corresponding to the source location is

designated as 0°. The angular increment of the detectors was made in steps of 10°

10   proceeding in a clockwise direction.

Definition of Sensitivity and Resolution

Sensitivity is defined as the relative intensity change between a defined target

medium and a "background" medium from which the embedded object(s) is/are removed

and replaced by material having the same properties as the bulk of the target medium.

15   Thus, in the equation below, u_t and u_b represent the photon intensities produced at a

detector by the target and by the background medium, respectively. Accordingly, the

computed relative intensity change (i.e., sensitivity) is:

$$\delta_u = 1 - \frac{u_t}{u_b}$$

Resolution is defined as the edge-spread function, corrected for the expected

20   influence of the tumor geometry. Resolution is thus equal to the excess of the full–width

at half–maximum (FWHM) of the sensitivity curve above its theoretical minimum value,

(i.e., EFWHM = FWHM − FWHM$_{geom}$). Here, FWHM$_{geom}$ = 2sin^{-1}(r/R), where r and R

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respectively are the radii of the centered inclusion and of the medium, as illustrated in

FIG. 6. Therefore, a decrease in EFWHM signifies an improved resolution, whereas an

increase in EFWHM means a loss of resolution. While this definition is valid, it is

correct in absolute terms only in cases of comparisons between breast maps having the

5   same diameter. On the other hand, in comparisons made among media of different

diameters, a variation in the EFWHM is evidence of a change in the edge resolution

relative to the size of the medium.

Parameter Space

The analysis examined the dependence of object sensitivity and edge resolution

10   on four of seven principal parameters directly associated with the measurement and target

domains. The corresponding dependences were inferrable for the other three parameters,

because of known relationships among the seven. Principal parameters that were directly

examined were variations in breast and tumor size, background tissue and tumor contrast,

and the influence of view angle and source position. Inferred parameters were the impact

15   of structural heterogeneity, choice of illuminating wavelength and use of contrast agents.

In each case, the analysis considered a range of parameter values in an effort to better

define their influence on the computed sensitivity and edge resolution.

Table 1 lists the diameters of the breast maps and tumors explored. These values

were selected on the basis of the expectation that tumors can be located almost anywhere

20   in the breast, from near the nipple to the chest wall, and that breast and tumor size

obviously vary. For each of the seven breast diameters examined, the analysis

additionally explored five different cross-sectional areas occupied by the tumor.

Case #	Breast Diameter (cm)	Tumor Diameter (cm) [Corresponding to (Ratio of Tumor Cross-sectional Area to Breast Cross-Sectional Area) x 100]				
		0.0625%	0.25%	1%	2.25%	4%
I	16	0.4	0.8	1.6	2.4	3.2
II	12	0.3	0.6	1.2	1.8	2.4
III	10	0.25	0.5	1.0	1.5	2.0
IV	8	0.2	0.4	0.8	1.2	1.6
V	6	0.15	0.3	0.6	0.9	1.2
VI	4	0.1	0.2	0.4	0.6	0.8
VII	2	0.05	0.1	0.2	0.3	0.4

TABLE 1: Diameters of Breasts and Embedded Tumors

Table 2 lists the optical coefficients assigned to an embedded tumor. The values were selected based primarily on reports in the literature regarding observed optical properties of excised normal and cancerous breast tissue (T. L. Troy, D. L. Page, D. L.

5 and E. M. Sevick–Muraca, "Optical properties of normal and diseased breast tissues: Prognosis for optical mammography," J. Biomedical Optics 3, 342–355 (1996)) (the disclosure of which is incorporated herein by reference). In some cases a more extended range was adopted, in order to explore the potential influence of contrast agents. For each of the composite breast/tumor sizes considered, the analysis considered the effect

10 that variations in tumor contrast have on sensitivity and edge resolution. This parameter (i.e., variations in tumor contrast) was subdivided into three different contrast ranges. In two of these the scattering contrast was varied in the presence of moderate and high, but in either case fixed, absorption levels, and in the third the absorption was varied in the presence of a typical, fixed scattering value. In total, seven different contrast levels were

15 explored.

Group	Case #	μ_a (cm^{-1})	μ_s' (cm^{-1})
(A)	5, 6, 7	0.08	40, 20, 10
(B)	1, 2, 3	0.2	40, 20, 10
(C)	7, 3, 9	0.08, 0.2, 0.4	10
(D)	4, 8	0.2, 0.08	5

Table 2: Optical Properties of Tumor Tissue

The range of contrast values assigned to the background tissues is shown in Table 3. Three different ranges of coefficient values were explored here, as well. These correspond to variations in the background absorption and scattering coefficients of the adipose tissue, and in the scattering coefficient of the parenchymal tissue. For comparative purposes we also explored the homogeneous state, as it represents the lower limit of contrast variation for the background tissues. In all, eight different background types were explored for each of the previously mentioned tumor contrast values. In total, the complete parameter matrix explored amounted to nearly 2,600 cases for each source location examined. The majority of these cases involved situations wherein the embedded tumor had higher absorption and/or scattering coefficient values than those of the background medium. It deserves emphasis that whereas we also have explored other MRI breast maps, all results reported here for inhomogeneous media are derived from a single MRI map.

Group	Case #	Adipose		Parenchyma	
		μ_a (cm^{-1})	μ_s' (cm^{-1})	μ_a (cm^{-1})	μ_s' (cm^{-1})

Homogeneous	1	0.04	10	0.04	10
(A)	2, 3, 4	0.02, 0.04, 0.08	10	0.08	7
(B)	3, 7, 8	0.04	10, 15, 25	0.08	7
(C)	5, 6	0.04	10	0.08	15, 25

Table 3: Optical Properties of Background Tissue

In review the results, the limiting case of contrast variation in breast maps with homogeneous backgrounds is considered first.

5   **Influence of Target Size**

The angular dependence of the relative intensity change on the size of the homogeneous background (i.e., breast) for a fixed inclusion (tumor) contrast value and fixed ratio of inclusion area to target area is shown in FIG. 7. The target diameter was varied between 2 and 16 cm to cover the expected range of diameters in the vicinity of

10   the nipple and chest wall. The analysis shows that, contrary to what one might expect, the analysis shows that in all cases studied an increase in the total path length of the medium, corresponding to an increase in target size, significantly enhances the maximum relative intensity change observed at larger angular distances from the source. At intermediate angular distances, a biphasic response is observed (i.e., as the total path

15   length increases, sensitivity at first rises, then falls).

Also shown in FIG. 7 is the seemingly counterintuitive finding of a reduction in the width of the sensitivity response curve with increasing target size. This indicates that an improvement in edge resolution accompanies the enhancement in sensitivity seen upon increasing the total path length. It is worth noting that these effects are not widely

20   appreciated, although as shown elsewhere, they are predictable from theoretical

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considerations (H. L. Graber, R. Aronson, and R. L. Barbour, "Dependence of object sensitivity and resolution on optical thickness of scattering media," _J. Optical Society of America A_, submitted) (the disclosure of which is incorporated herein by reference). Also, note that because the comparison in sensitivity is between maps of different sizes,

5   the enhancement seen in edge resolution is in relative terms. These responses are quantified in more detail in FIGS. 8A and 8B.

Effect of Composite "Breast/Tumor" Size on Sensitivity and Edge Resolution

Further examination of the above–described phenomenology is shown in FIGS. 8A and 8B, and 9A and 9B. Here the analysis has computed the maximum relative

10   intensity change for a detector positioned 180° from the source (FIGS. 8A and 8B) and the corresponding excess of the full-width at half-maximum (EFWHM) (FIGS. 9A and 9B), as a function of the composite breast/tumor geometry, for a fixed tumor contrast. A comparison of results in FIGS. 8A and 9A shows that an increasing the ratio of the cross–sectional area of the tumor to that of the breast with the breast diameter fixed increases

15   sensitivity significantly, especially for larger breast sizes (cf. FIG. 8A), and improves edge resolution slightly (cf. FIG. 9A). Results in FIGS. 8B and 9B demonstrate the corresponding response to variations in the breast diameter with a fixed ratio of cross-sectional areas. Again, a positive correlation is seen between sensitivity and target size when either one of the size parameters is fixed. Interestingly, the maximum rate of

20   sensitivity change occurs when extreme values of the target geometry are paired. That is, the greatest change in sensitivity values occurs with large breasts containing small tumors (a clinically interesting case) (FIG. 8A) and small breasts containing large tumors (FIG.

8B). These findings indicate that sensitivity responses do not simply scale with target size.

**Influence of Composition of Target Geometry and
Tumor Contrast on Sensitivity vs. Edge Resolution**

5   The results in FIGS. 10A through 10C show the EFWHM versus the maximum sensitivity for the detector positioned 180° from the source, as functions of breast size, tumor–to–breast area ratio and tumor contrast, for the different contrast groups. In FIGS. 10A and 10B the absorption coefficient of the tumor is fixed at 0.08 cm^{-1} and 0.2 cm^{-1}, respectively, and the scattering coefficient varies from 10 to 40 cm^{-1}. In FIG. 10C the

10   scattering coefficient of the tumor is fixed at 10 cm^{-1} and the absorption coefficient varies from 0.08 to 0.4 cm^{-1}. Shown are the responses for three different area ratios (labeled A, B, and C, where A corresponds to 0.0625%, B to 1.0%, and C to 4%), as a function of breast diameter. For each line drawn, the maximum sensitivity increases monotonically with increasing breast diameter, while at the same time the EFWHM monotonically

15   decreases.

         Most striking is the strong dependence of edge detection and sensitivity on breast size, especially for the smaller tumors. In this case, an increase in breast size preferentially enhances edge resolution, independent of tumor contrast. Increasing tumor size (groups A through C) with the breast size and tumor contrast fixed primarily

20   enhances sensitivity, although some enhancement in edge resolution is observed for larger tumors. Comparing results in FIGS. 10A through 10C illustrates the effect of varying tumor contrast. Results in FIG. 10A show that at moderate absorption values (i.e., 0.08 cm^{-1}), increasing the scattering contrast of the tumor preferentially enhances edge resolution for small breast sizes, while improving sensitivity for larger breast sizes.

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This differential response is most noticeable for breasts containing larger tumors. Results in FIG. 10B show that the sensitivity enhancement seen in large breasts when the scattering contrast of the tumor is increased is completely abolished upon increasing the absorption contrast of the tumor to 0.2 cm^{-1}. This shows that under the conditions

5   examined, a four–fold enhancement in scattering contrast of the tumor has no additional influence on its detectability. Results in FIG. 10C show that the greatest improvement in sensitivity is observed upon an increase in the absorption of the tumor, with the largest effect occurring with larger tumors.

The next analysis considers an inhomogeneous background (i.e., the anatomically

10   accurate optical (AAO) Breast Model).

Effect of Increased Background Scattering

In this section the analysis considered results obtained from the AAO maps. The point of this analysis was to determine if the presence of an inhomogeneous background can appreciably influence the sensitivity or edge resolution obtained for the included

15   tumor, relative to the homogeneous case. Results shown in FIG. 11 illustrate the effect that an increase in the difference between scattering coefficients of adipose and parenchymal tissue has on sensitivity, for the case of a small tumor (0.25% ratio of cross–sectional area) embedded in a large breast (16 cm). Specifically shown are responses seen for Groups B and C background media, which differ in the direction of the scattering

20   contrast between the adipose and parenchymal tissues. For comparative purposes, the response seen for a homogeneous background also is shown. The most noticeable effect of background heterogeneity is a shift in the angle at which the greatest sensitivity is observed. Interestingly, the direction of this shift depends on the algebraic sign of the

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difference between the background tissues' scattering coefficients. The angle of

maximum sensitivity is >180° when the adipose tissue is more strongly scattering than

the parenchyma, and <180° when the parenchyma is the more strongly scattering. The

ratio of maximum sensitivity to sensitivity at precisely 180° can be greater than 2:1, a

5   result that highlights the limited value that restricted–view measurements can have for

inhomogeneous media. Also seen in FIG. 11 is a marked reduction of the EFWHM for

the medium having the largest scattering contrast between adipose and parenchymal

tissues, especially for the Type–6 background, indicating improved edge resolution.

Not shown are results of similar analyses wherein the tumor size and contrast

10   were varied as a function of background tissue contrast. In cases involving comparisons

between media with similar tumor–to–breast area ratios, the influence of variations in

tumor contrast, for a specified background, were mainly quantitative in nature. That is, in

those situations where the above–described view–angle dependence of sensitivity on

background scattering contrast was observed, it was largely independent of tumor

15   contrast. This indicates that the observed behavior is primarily a function of the

background contrast. Quantitatively, reduction in the absorption or scattering contrast of

the included tumors predictably reduces measurement sensitivity. The influence of breast

size on the angular response function is shown subsequently.

Influence of Breast Size

20   The results illustrated in FIG. 12 show the effect on sensitivity of varying the

breast size while holding the tumor–to–breast area ratio fixed, for a selected

heterogeneous background medium (i.e., Case 6 background). A similar plot for the

homogeneous background case was shown in FIG. 7. Comparison reveals that whereas

the edge resolution improves with increasing breast size also in this heterogeneous case, its angular dependence is not a simple function of breast size. This absence of linear scaling between measured response and target geometry can be seen more clearly by comparing the sensitivities observed at 180° and at 200° view angles, as a function of the

5   composite breast/tumor size. These results are shown in FIGS. 13A and 13B. In FIG. 13A the analysis shows a strong, nearly linear dependence of angular sensitivity on tumor size for large–diameter breasts but very little dependence for small–diameter breasts, even though the exact same heterogeneous background structures are present. FIG. 13B further shows that, in addition to this lack of scaling, the angular sensitivity dependence

10   varies with tumor size, with the greatest dependence observed in the case of the smallest tumor embedded in a large breast (a clinically interesting case).

Influence of Source Location

The results in FIGS. 14A and 14B show the dependence of the maximum sensitivity on source location (0° vs. -40°), as a function of the tumor cross–sectional

15   area and the breast diameter, for background medium 6. This comparison is made to model how the source location influences the expected sensitivity of measurement for a heterogeneous medium, as a function of composite target geometry. Inspection of FIGS. 14A and 14B reveals trends similar to those observed in FIG. 13A and 13B. Thus, whereas it is to be expected that varying the source position can influence measurement

20   sensitivity for a heterogeneous medium, what is not obvious is that the magnitude of the differential response is dependent on the composite target geometry. The form of this dependence reveals an absence of scaling in sensitivity as a function of composite target geometry, even though identical background structures are present.

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**Comparison of Sensitivity Dependence of
MRI Breast Map to Homogeneous Background**

Results in FIGS. 11 through 14 identified the sensitivity dependencies of various

measurement configurations for a fixed structural heterogeneity, as a function of

5   background contrast and of composite target geometry. To complete our understanding,

it is useful to isolate the influence of structural heterogeneity per se. This was

investigated by comparing the measured responses for the case 6 background to those for

a homogeneous background medium (case 1), as a function of composite target geometry,

for a detector positioned opposite the source (i.e., 180° view angle). FIGS. 15A and 15B

10   show the result for the case of type–3 tumor contrast, as a function of the composite

target geometry. In FIG. 15A, we see that compared to the homogeneous case, the

influence of structural heterogeneity on the detectability of the tumor varies strongly with

breast size. For small–diameter breast maps, the presence of added contrast between the

parenchyma and adipose tissues improves sensitivity to the tumor. However, the

15   opposite effect is seen for larger diameter breasts, even though the identical structural

heterogeneity and contrast difference is present in all cases, further demonstrating an

absence of scaling in the measured response with target size. FIG. 15B shows a similar

dependence when tumor size is varied.

**Influence of Composition of Target Geometry and
20   Tumor Contrast on Sensitivity vs. Edge Resolution**

The results in FIGS. 16A through 16C show the effects of variations in the target

geometry on EFWHM and on relative sensitivity at the 180° view angle, for the three

tumor contrast ranges and a selected inhomogeneous background (i.e., type 6). A similar

study for a homogeneous background is shown in FIGS. 10A through 10C. Comparison

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of data in FIGS. 10 and 16 reveals that while qualitative similarities are present, overall a more complex response is seen in the heterogeneous case. Most notable is that portions of some of the EFWHM vs. sensitivity relations are not single-valued functions, revealing that in these cases maximum sensitivity is achieved at some intermediate breast

5   size. Also different is the loss of edge resolution with increasing tumor size, especially in the case (FIG. 16C) of variable tumor absorption coefficient. It is worth noting that results presented in FIG. 16 do not coincide with the position of maximum sensitivity, which as shown in FIG 12, occurs at a ~200° view angle from the source. A similar analysis at this view angle (results not shown) produced trends closer to those observed

10   for a homogeneous medium. This suggests that background heterogeneity per se does not fundamentally limit the achievable edge resolution and sensitivity, but instead alters the location where they can be attained.

Response to Reduced Contrast Tumors

The results presented in the preceding figures emphasize mainly the influence that

15   the various parameters have on the computed responses for tumors having higher absorption and scattering coefficients than those of the surrounding background medium. In FIGS. 17A through 17D, we examine the corresponding responses for a case in which a tumor is more weakly scattering than the background, for different breast sizes, and compare this to the homogeneous case. Overall, we see that while in many cases a more

20   complex profile is observed, the trend favors improved sensitivity and improved edge detection with increased breast size.

Summary of the Principal Results

An important phenomenon observed in the results presented is that for any tumor—to—breast area ratio, tumor contrast and background medium contrast, the maximum sensitivity and edge resolution both increase significantly as the breast diameter

5   increases. Also observed is that increasing the tumor size, for a fixed tumor contrast and breast size, increases sensitivity and, to a lesser extent, edge resolution (cf. FIGS. 9, 10 and 16). In addition, increasing the absorption contrast of the tumor alone increases sensitivity, but does not improve edge resolution (cf. FIGS. 10, 16).

We also observed that the effect of varying the scattering contrast of the tumor on

10   sensitivity and edge resolution is a function of composite target size as well as of the absorption contrast of the tumor (cf. FIGS. 10, 16). For small breasts, sensitivity and edge resolution are improved simultaneously as the scattering contrast of the tumor increases, but there is a larger change in sensitivity for small breasts with a large tumor. For large breasts the effects on edge resolution and sensitivity are different, such that

15   increases in the scattering contrast of the tumor improves sensitivity alone, but only with tumors having moderate absorption contrast.

In all, a consistent finding throughout all the variations explored is the absence of scaling of the measured response with target size. Specifically, we mean that trends observed in edge resolution and sensitivity as a function of tumor contrast, size and

20   background contrast do not extrapolate to media of larger sizes, even though the exact same distribution of internal contrast and tumor size relative to background medium is present. These findings not only provide a comprehensive understanding of expected measurement performance associated with the two types of parameter spaces explored, (i.e., measurement and target domains), but also provide a guide to identifying the optical

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measurement strategies required to obtain optimal sensitivity and resolution. In the

following, we extend these observations and discuss complementary strategies that can

optimize achievable sensitivity and resolution.

Discussion

5   We have systematically explored the parameter domains associated with the target

properties and measurement conditions, for the purpose of gaining insight into the

relationships between these domains and their possible influence on the design of

practical imaging systems. Two critical parameters that should be kept in mind when

designing such systems are expected limits on sensitivity and resolution. Without a

10   doubt, an important factor influencing these limits will be the view angle of

measurement. In the case of imaging studies on the breast, several options are available,

some of which have been adopted without rigorous proof that they are best suited for

achieving optimal sensitivity and resolution.

One design in particular that has been implemented is a raster scan with a single

15   detector positioned 180° opposite the source, with the breast subjected to mild planar

compression. While compression of the breast will improve signal levels, it will be at the

expense of a restricted view. Results in FIG. 12 show that, depending on the optical

properties of the background tissues and their distribution in relation to a region of

interest (ROI), sensitivity to a centrally located structure can vary several–fold over an

20   angle of 20°. Since details of the underlying structural heterogeneity of the breast are

unknown a priori, the influence of such structures on sensitivity can be expected to vary

significantly. At a minimum, this observation suggests that the presence of

heterogeneous backgrounds in the breast will severely limit efforts to obtain reproducible

results from measurements employing restricted views. This would be especially true should serial measurements be performed, in which case the plasticity of the breast would surely undermine efforts to reproduce precise positioning of the tissue.

Our results suggest that improved reproducibility should be achievable using

5   measurement schemes that employ broader views, because background heterogeneity can shift the location where optimal sensitivity is achieved. The difficulty with this approach is that it may limit the ability to use planar compression schemes. As indicated, while it is clear that compression of the tissue will improve signal levels, it is worth examining whether this is accompanied by improvements in sensitivity and resolution. Although

10   planar compression geometries were not specifically investigated in this study, we believe that comparison of results from the different breast sizes can nevertheless provide insight into the expected influence of such geometries on these parameters.

Comparison of results for different model diameters is equivalent to imposing radial compression on the tissue, because the internal features of the different breast

15   models studied are identical to a first approximation. Table 4 lists results derived from FIGS. 8A and 8B, and 9A and 9B, where the expected influence of a radial compression maneuver on sensitivity and edge resolution of the tumor is examined assuming different compression responses of an included tumor. For simplicity, expected out–of–plane effects of tissue/tumor compression are ignored. Considered is a large breast (16 cm)

20   containing a tumor whose size (1.6 cm) is 1% of the total cross–sectional area. These results show that use of compression techniques is always accompanied by a loss of resolution due to reduced breast size, while its effect on sensitivity depends on the degree of compressibility of the tumor with respect to the surrounding tissue. In the case where

the tumor has compressibility similar to that of the surrounding media, radial

compression of the tissue from 16 cm to 10 cm diameter causes a 29% and 35% loss of

sensitivity and edge resolution, respectively. These values compare to corresponding

declines of 16% and 34% for the case of partial tumor compression, and to a 25% gain in

5   sensitivity coupled with a 31% loss of resolution for an incompressible tumor. These

results show that tissue compression per se does not guarantee improvement in sensitivity

and resolution, and frequently can make matters worse.

Items	Before Compression	After Compression		
Breast Diameter (cm)	16	10		
Tumor Diameter (cm)	1.6	1.0 (Proportionally Changed)	1.4	1.6 (Completely Unchanged)
Tumor-to-Breast Area Ratio (%)	1	1	1.96	2.56
Maximum Sensitivity (%)	39.1	27.6 (↓ 29.4%)	33.0 (↓ 15.6%)	49.0 (↑ 25.3%)
Resolution (EFWHM) (Degrees)	58.36	78.92 (↓ 35.2%)	78.11 (↓ 33.8%)	76.73 (↓ 31.48%)

10   Table 4: Influence of a Radial Compression Maneuver on
                                Sensitivity and Edge Resolution

Although illustrative embodiments have been described herein in detail, those

skilled in the art will appreciate that variations may be made without departing from the

spirit and scope of this invention. Moreover, unless otherwise specifically stated, the

15   terms and expressions used herein are terms of description and not terms of limitation,

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and are not intended to exclude any equivalents of the system and methods set forth in the

following claims.

What is claimed is:

1.   A method for collecting data for use in image reconstruction of a scattering target medium, comprising:

providing a source for directing at least one wavelength of energy into a target medium;

providing a detector for measuring energy emerging from the target medium;

selecting at least one wavelength of energy, wherein at least one wavelength of energy is selected to maximize the total path length of energy propagating from the source to a detector and to maintain an acceptable energy density at the detector;

directing at least one selected wavelength of energy into the target medium; and

measuring at least one wavelength of energy emerging from the target medium.

2.   The method of claim 1, wherein the total path length is the sum of a plurality of total mean free path lengths a particle of energy travels as it propagates through the medium from the source to a detector.

3.   The method of claim 1, wherein a single detector is provided.

4.   The method of claim 1, wherein a plurality of detectors are provided at a plurality of distances from the source.

5.   The method of claim 4, wherein a single wavelength is selected, the wavelength being selected to maximize the total path length of energy from the source to

a detector furthest from the source and to maintain an acceptable energy density at the farthest detector.

6.   The method of claim 5, wherein the farthest detector is the detector having lowest energy density measurement among the plurality of detectors.

7.   The method of claim 5, wherein the farthest detector is the detector detecting the energy having the longest total path length among the total path lengths of the energy propagating from source to each of the plurality of detectors.

8.   The method of claim 4, wherein a plurality of different wavelengths are selected, each of the plurality of wavelengths being selected to maximize the total path length of energy from the source to a detector and to maintain an acceptable energy density at the detector.

9.   The method of claim 1, wherein selecting at least one wavelength comprises:

directing a wavelength of energy into the target medium;

measuring the emerging energy from the target with at least one detector; ·

adjusting the wavelength of the energy based on the measured emerging energy to maximize the total path length and to maintain an acceptable energy density at a detector; and

selecting at least one wavelength of energy having a maximized total path length from the source to at least one detector and an acceptable energy density at a detector.

10.   The method of claim 9, wherein the wavelength is adjusted to increase the total path length and decrease the energy density at a detector.

11.   The method of claim 9, wherein the wavelength is adjusted to decrease the total path length and increase the energy density at a detector.

12.   The method of claim 9, wherein the adjusting step is repeated until a wavelength is selected.

13.   The method of claim 9, wherein the adjusting step is repeated until a plurality of wavelengths are selected.

14.   The method of claim 1, further comprising radially compressing the target medium.

15.   The method of claim 15, wherein the radial compression is prior to selecting the at least one wavelength.

16.   The method of claim 15, wherein the target medium comprises a background medium and an object medium having different compressibility characteristics.

17.   The method of claim 16, wherein radially compressing the target medium causes greater compression of the background medium than of the object medium, so that a ratio of object medium to background medium is increased.

18.   A method of selecting an optimal wavelength of energy for imaging in a

scattering medium, comprising:

providing a source for directing at least one wavelength of energy into the target

medium;

providing a detector for measuring energy emerging from the target medium;

directing a wavelength of energy into the target medium;

measuring the emerging energy from the target with at least one detector;

adjusting the wavelength of the energy based on the measured emerging energy to

maximize the total path length and maintain an acceptable energy density at a detector;

and

selecting at least one wavelength of energy having a maximized total path length

from the source to at least one detector.

19.   The method of claim 18, wherein the wavelength is adjusted to increase

the total path length and decrease the energy density at a detector.

20.   The method of claim 18, wherein the wavelength is adjusted to decrease

the total path length and increase the energy density at a detector.

21.   A method for collecting data for use in image reconstruction of a

scattering target medium, comprising:

providing a source for directing at least one wavelength of energy into a target

medium wherein the at least one wavelength is selected to maximize the total path length

of energy propagating from the source to a detector and to maintain an acceptable energy density at the detector;

    providing a detector for measuring energy emerging from the target medium;

    directing at least one selected wavelength of energy into the target medium; and

    measuring at least one wavelength of energy emerging from the target medium.

22.   A system for enhanced imaging of a scattering target medium, comprising:

    means for selecting at least one wavelength of energy, wherein the at least one wavelength of energy is selected to maximize the total path length of energy propagating from the source to a detector and to maintain an acceptable energy density at the detector;

    a source for directing at least one wavelength of energy into a target medium; and

    a detector for measuring energy emerging from the target medium;

    a means for reconstructing an image of the properties of the target medium.

23.   A system for enhanced imaging of a scattering target medium, comprising:

    a source for directing at least one wavelength of energy into a target medium wherein the at least one wavelength is selected to maximize the total path length of energy propagating from the source to a detector and to maintain an acceptable energy density at the detector;

    a detector for measuring energy emerging from the target medium; and

    a means for reconstructing an image of the properties of the target medium.

FIG. 1

FIG. 2

3/16
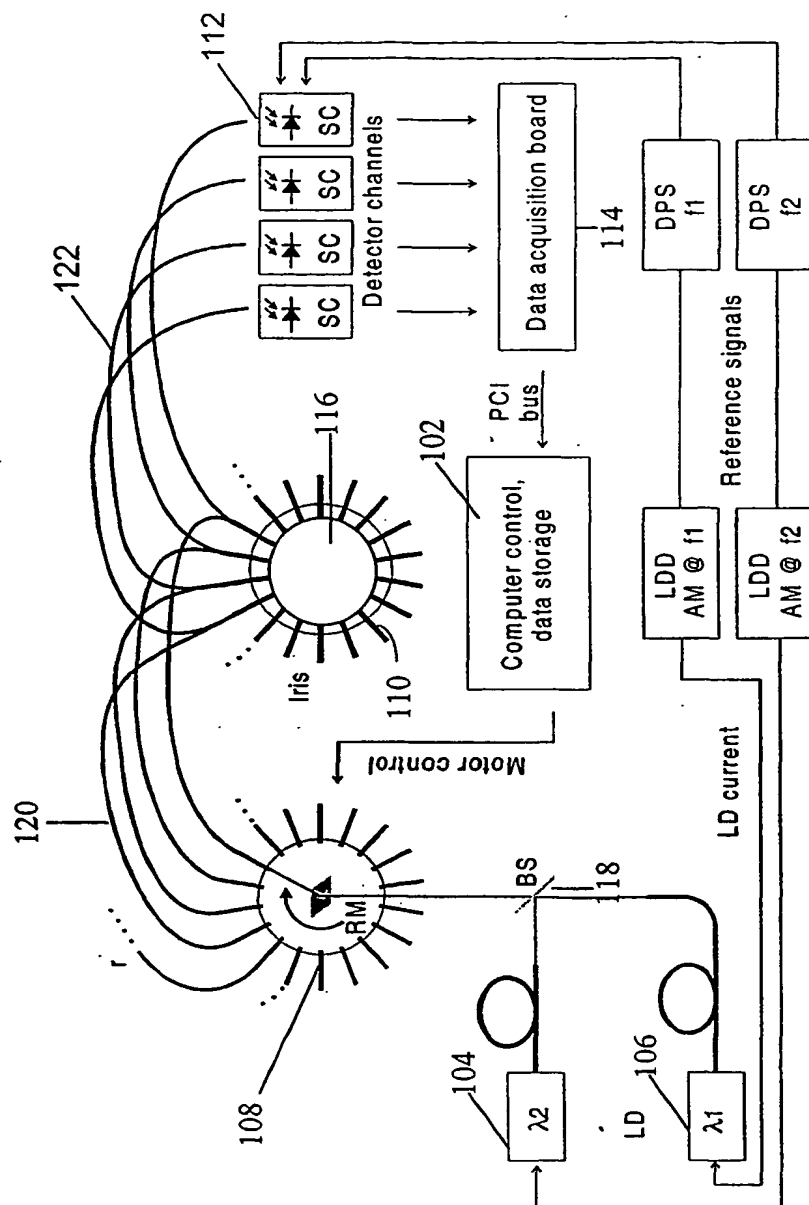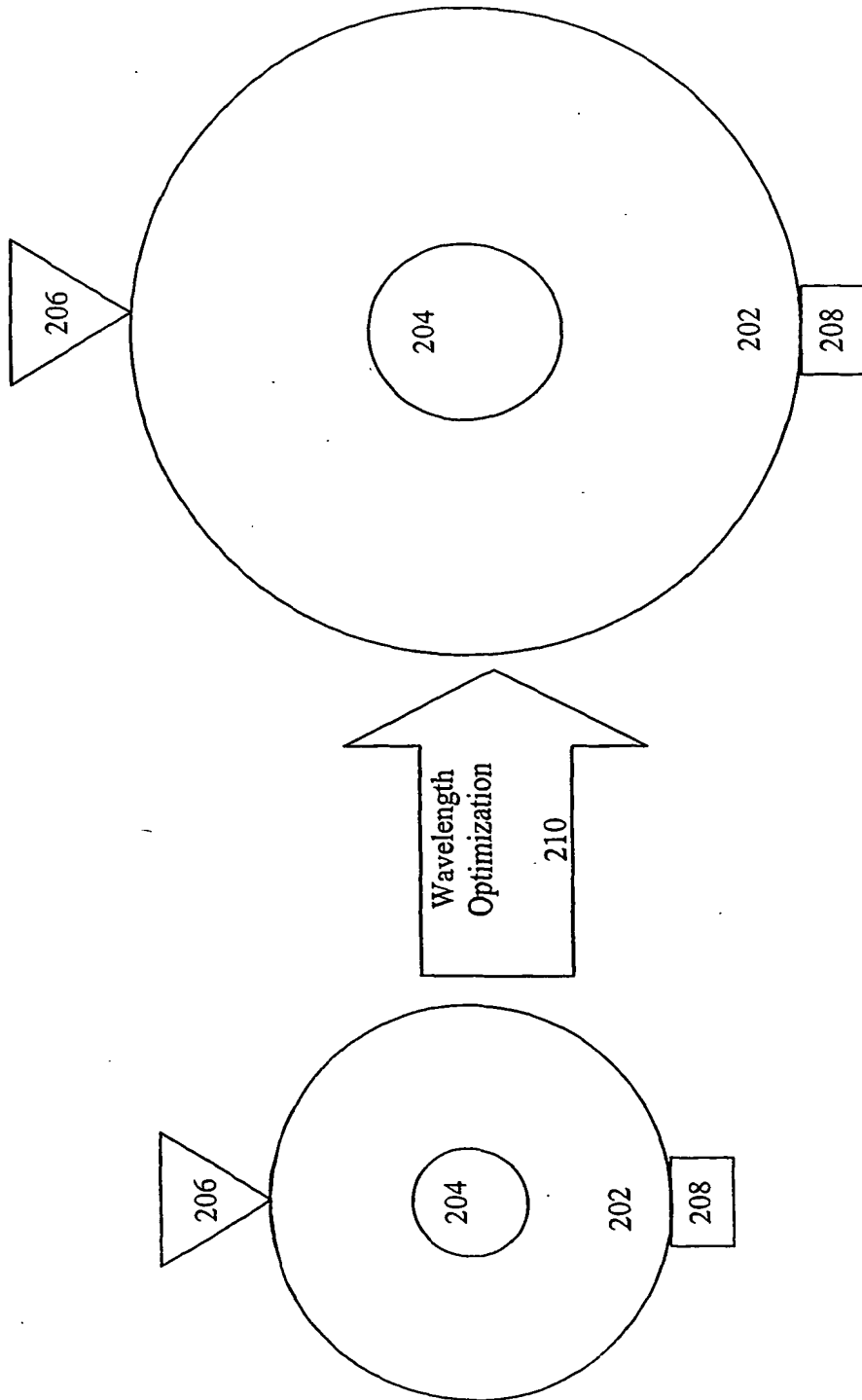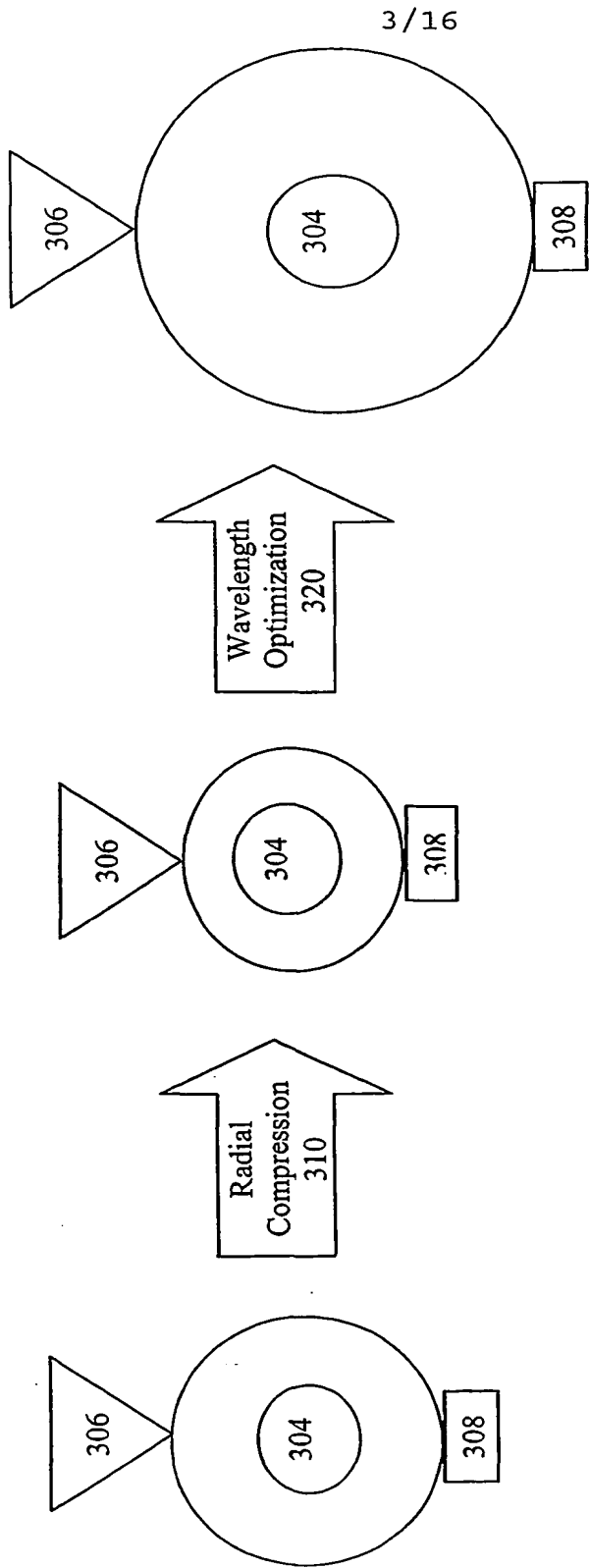
FIG. 3
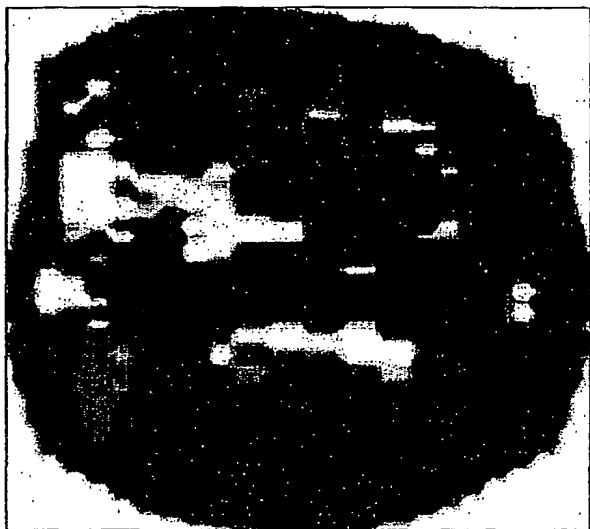
FIG. 4A
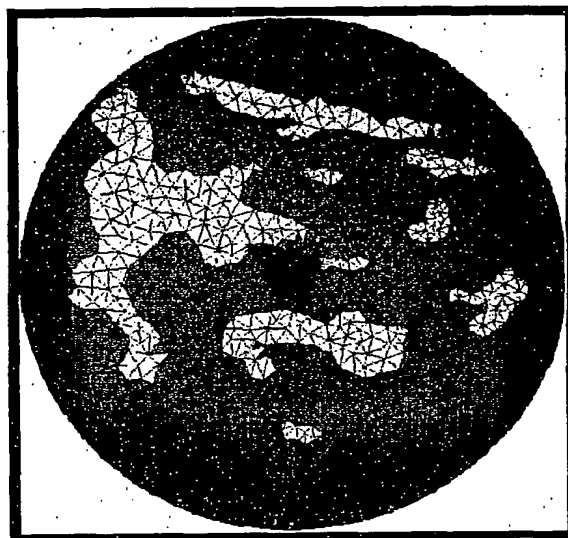
FIG. 4B
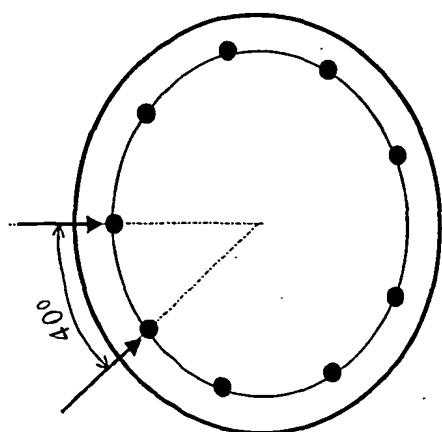
FIG. 6

FIG. 5
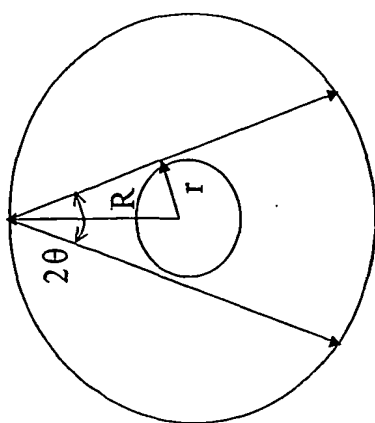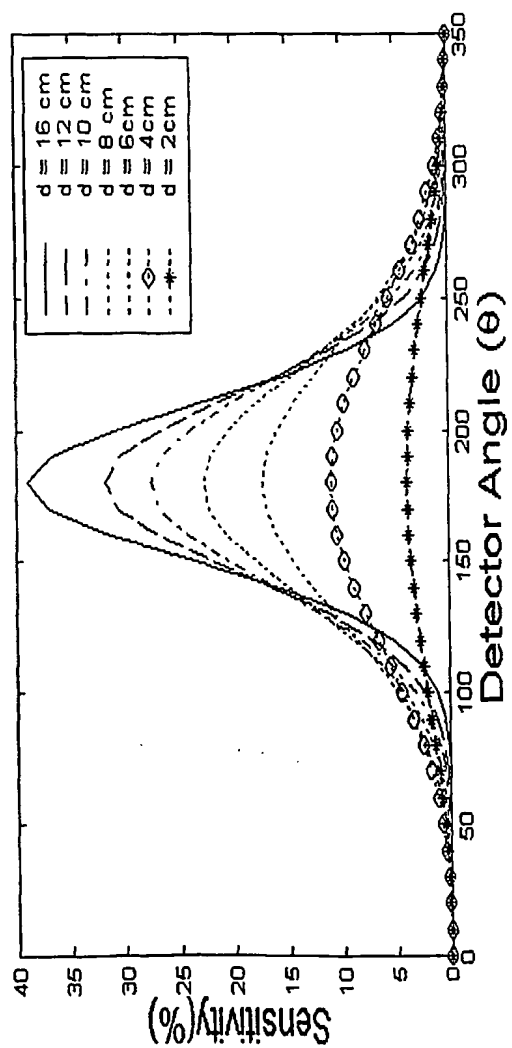
FIG.7
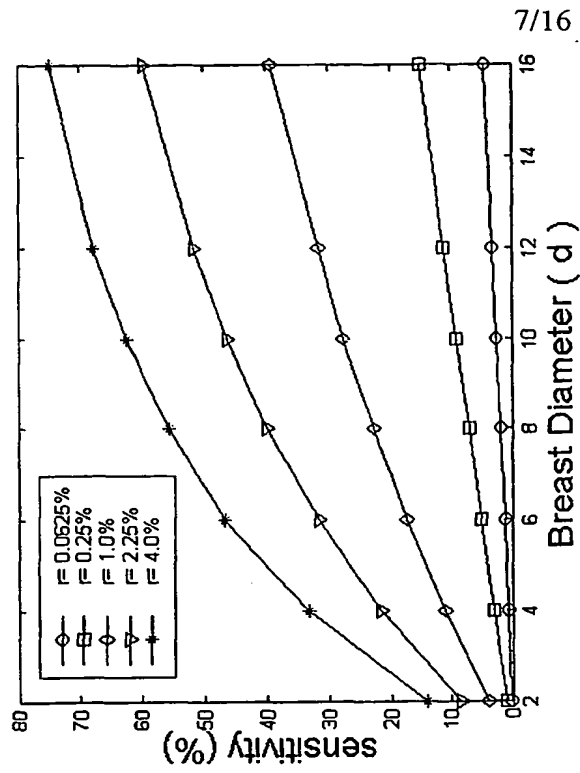
FIG. 8B
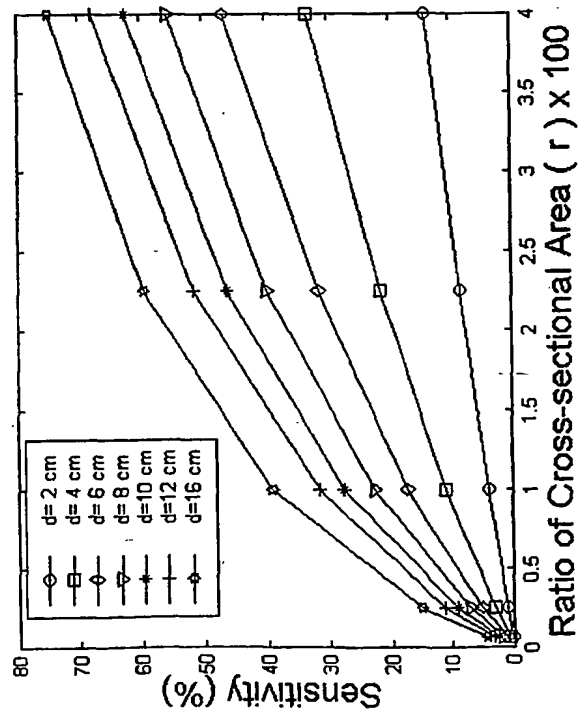
FIG.8A
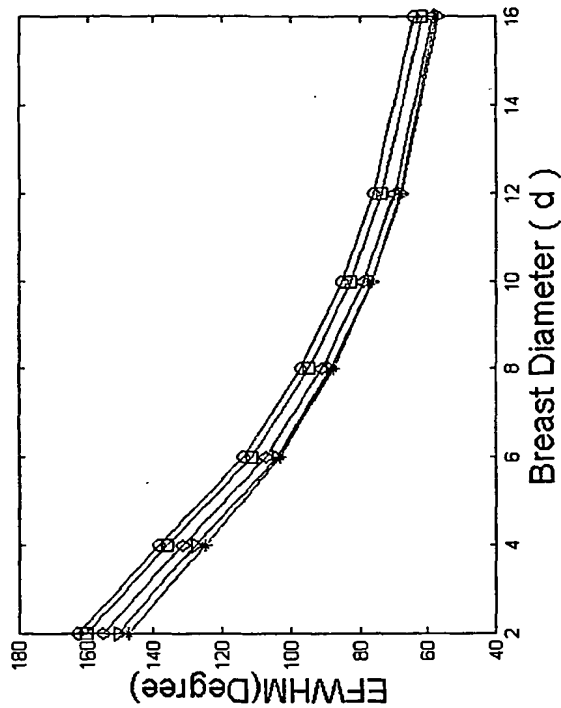
FIG. 9B
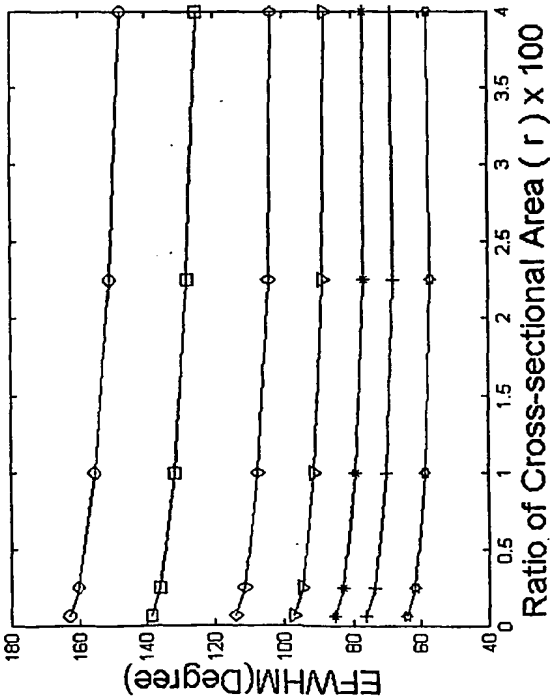
FIG.9A
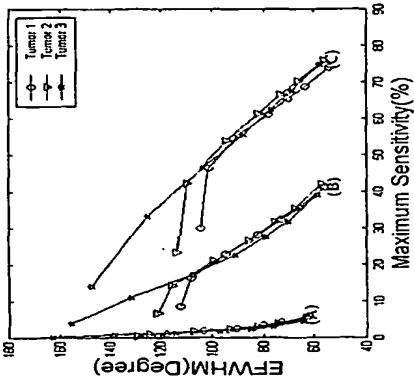
FIG 10B

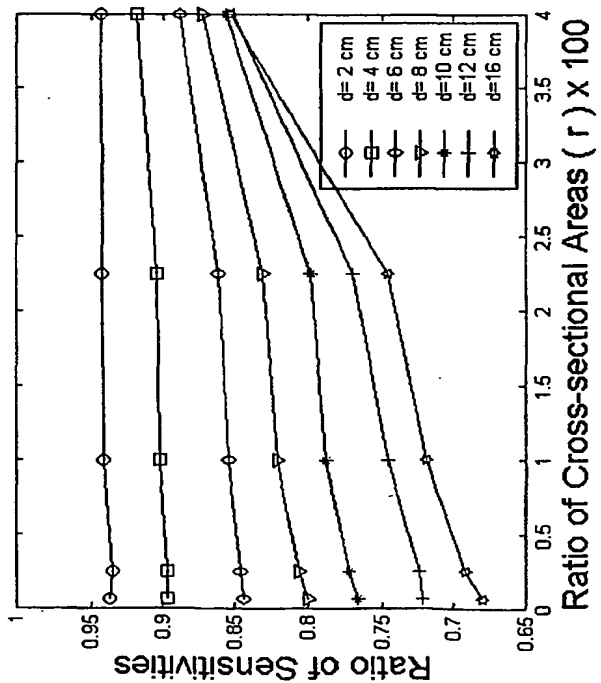

FIG 10A

FIG 10C
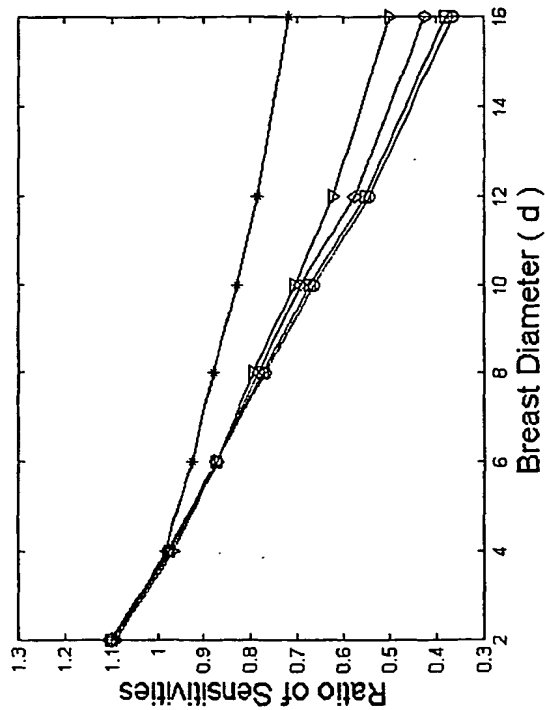
FIG. 12

FIG. 11
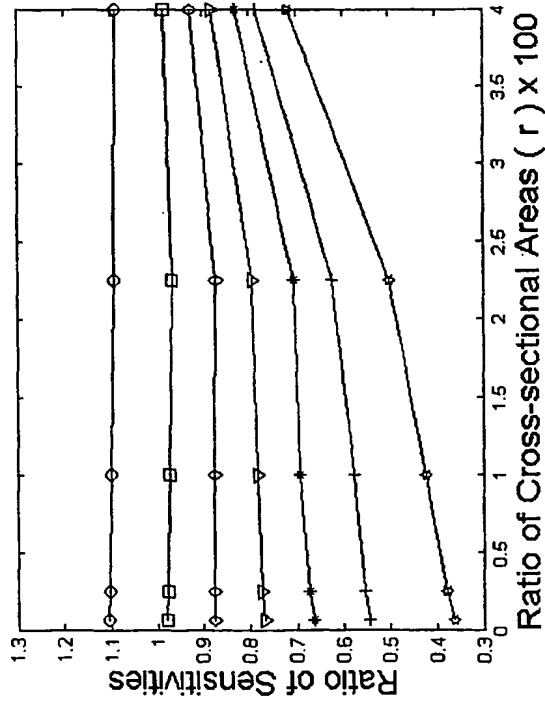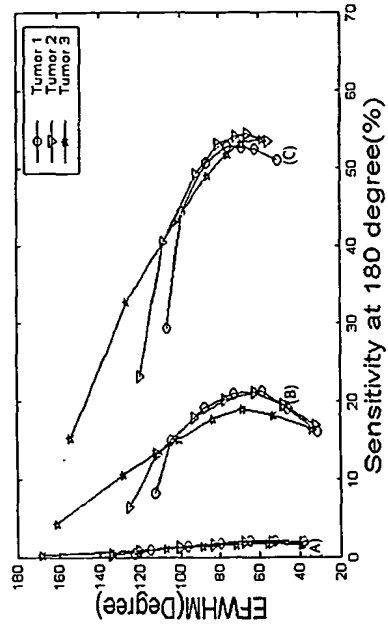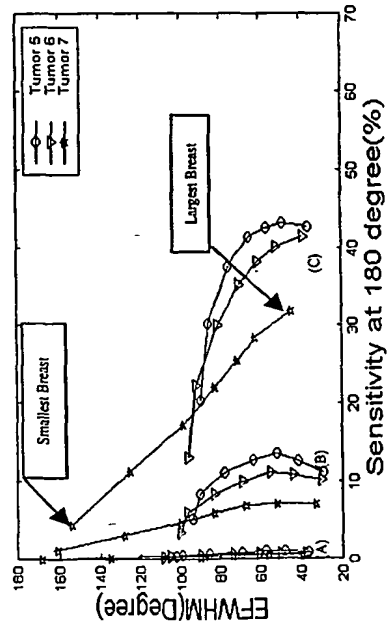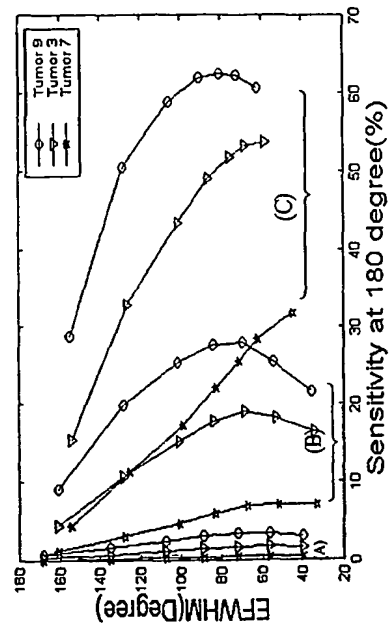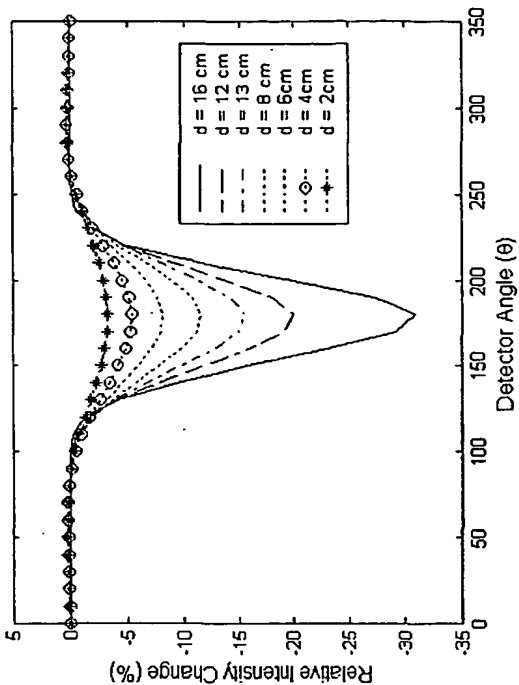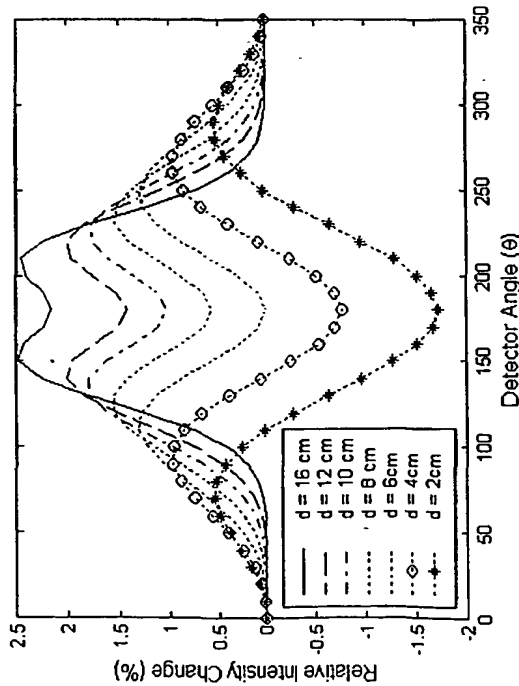
FIG. 13B

FIG.13A

FIG. 14B

FIG 14A

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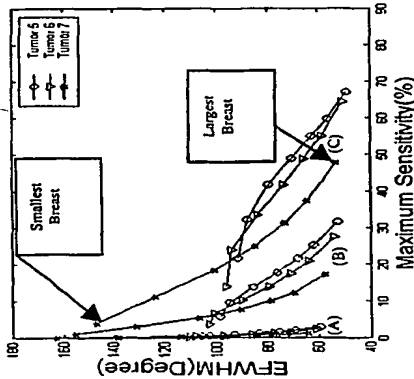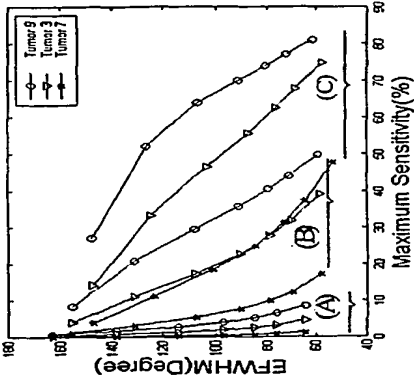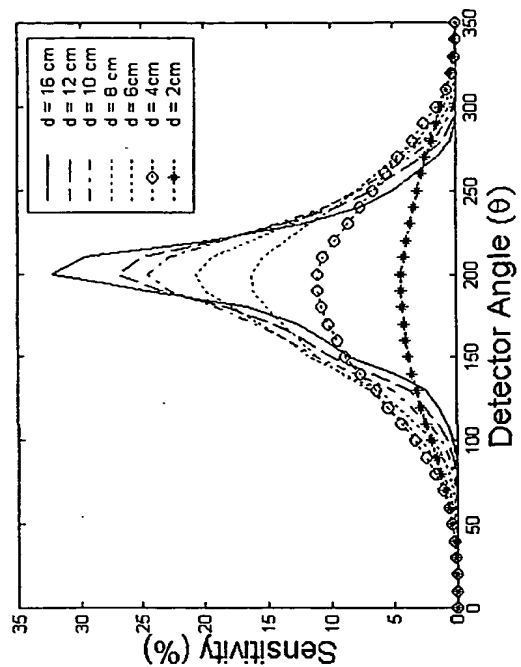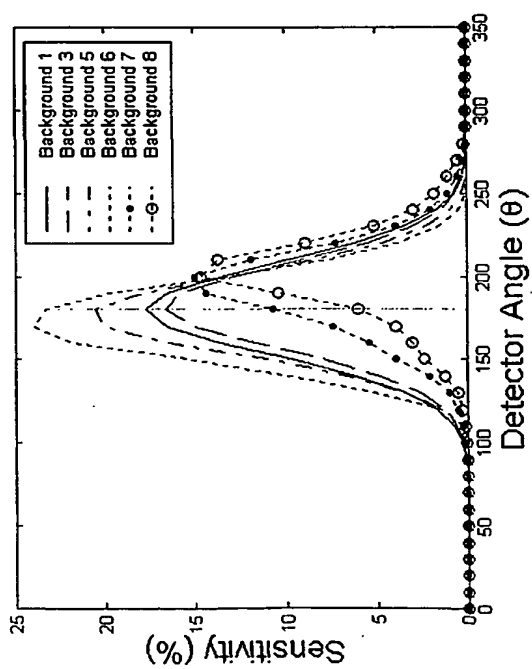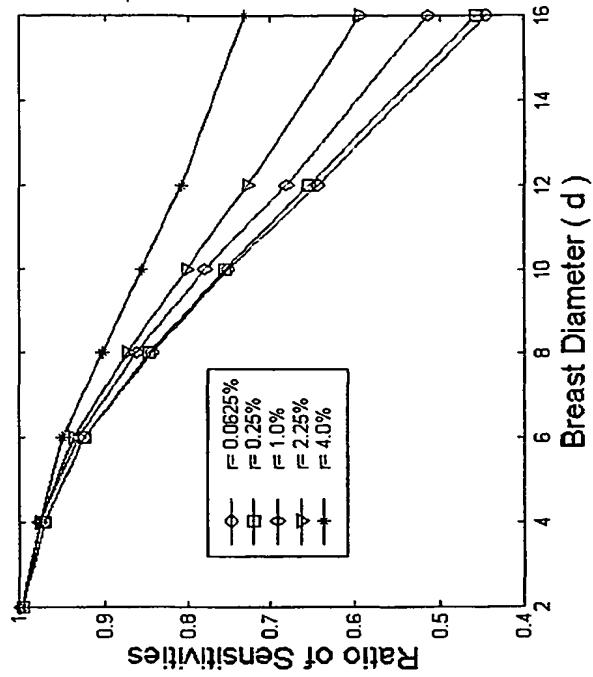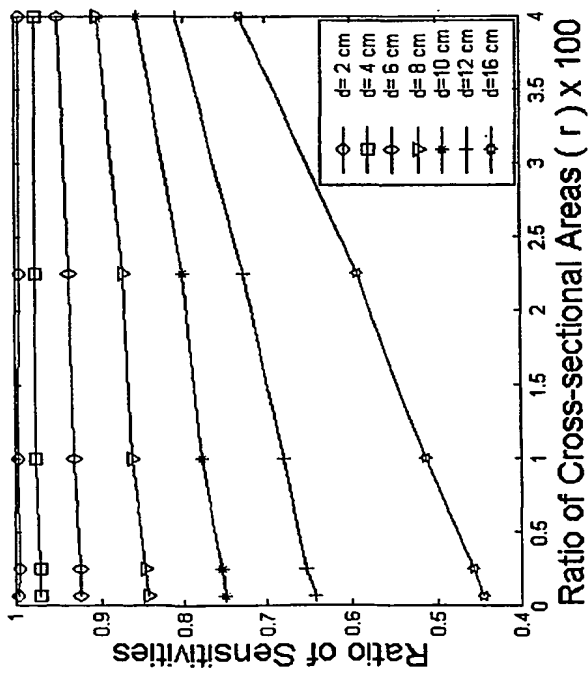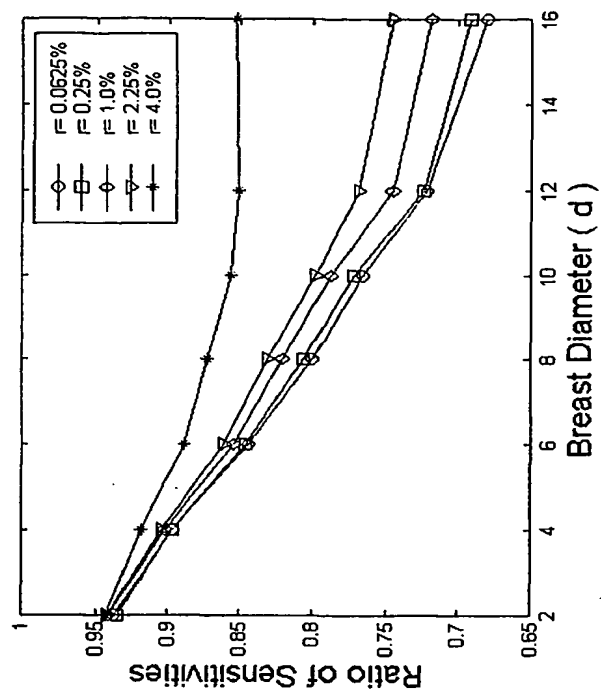
FIG. 15B

FIG 15A

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FIG. 16B

FIG. 16A

FIG. 16C

FIG. 17B

FIG. 17A

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FIG. 17D

FIG. 17C